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UNUSUAL PERIOSTITIS IN CHILDREN

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THESE five cases are reported, first, because of the close similarity of the x-ray and wide divergence of the clinical findings; second, to emphasize the value of co-ordinating the history and clinical findings in the interpretation of x-ray evidence, and third, because of the comparative rarity of some feature of each of these cases.

Three patients are from the Presbyterian Hospital of the City of Chicago, and two from the Central Free Dispensary of Rush Medical College of the University of Chicago.

All of the patients are children, ranging in age from six months to four and one-half years. Their x-ray films show on the shaft of long bones a fusiform elevation of periosteal new bone with dense, sharply defined calcification at the outer margin,

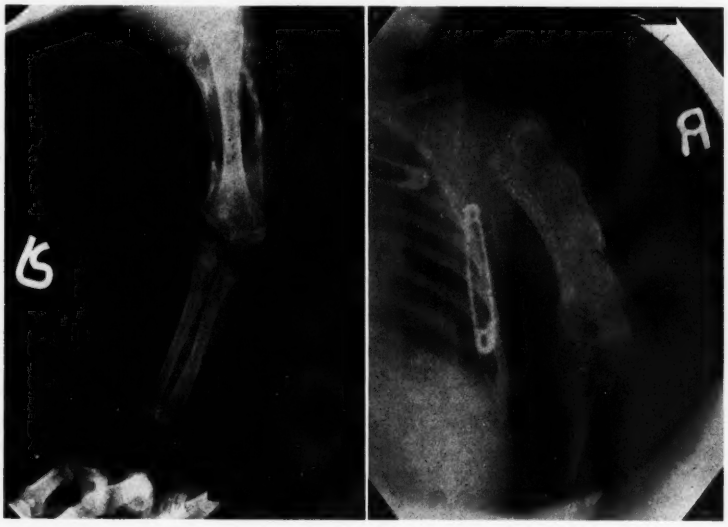

Fig. 1-*A*. Fig. 1-*B*.

Fig. 1-*A*. Case 1. Fusiform elevation of periosteal new bone of humerus, with well-defined shaft, slightly more dense than normal.
Fig. 1-*B*. Case 1. Film taken shortly after sequestrated shaft was removed *en masse* through incision in the involucrum.

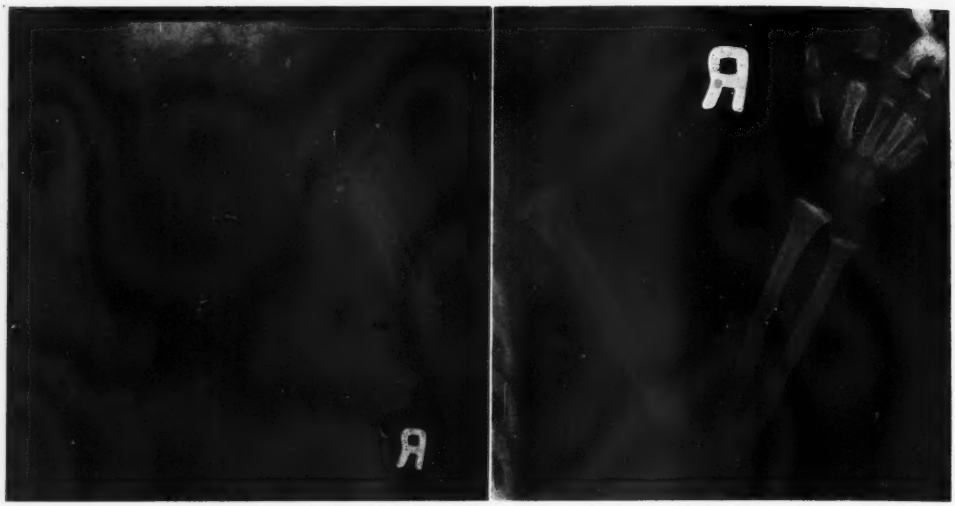

Fig. 2-*A*. Fig. 2-*B*.

Fig. 2-*A*. Case 2. Film shows periosteal new bone the entire length of both femurs, more markedly elevated in the upper half of each shaft, where it rises to a maximum of 2 centimeters. Subepiphyseal bone absorption has lead to displacement of the shaft at the upper end of both femurs. All of these changes are a little more marked on the right side and there is also marked swelling of the soft tissues of the right leg. The tibias and fibulas show these changes in less marked degree, accompanied by slight thickening of the metaphyseal margins.

Fig. 2-*B*. Case 2. Film of right upper extremity shows increased density at the epiphyseal margin of the lower end of the radius and ulna and slight thickening at the upper end of the humerus. There is no bone absorption and no periosteal new bone along the shafts.

which gradually decreases in density to the shaft. The bone shaft is distinctly visible and shows only slight change from normal. The lesions extend either a part or the entire length of the shaft. In four cases the lesions are multiple.

In the differential diagnosis of these cases from an x-ray standpoint, one must consider some process which is found in children, and which will elevate the periosteum. Hemorrhage or pus beneath the periosteum, such as can occur from trauma, scurvy, or osteomyelitis, a syphilitic or a rachitic periostitis, occasionally tumor, and more rarely tuberculosis, are lesions of this type.

Case 1. This is a white male child, six months old. A film of the right arm shows on the humerus a fusiform elevation of periosteal new bone from one epiphyseal line to the other, rising to a maximum height of one centimeter above the shaft. The calcification beneath the periosteum is homogeneous in character and gradually fades out toward the shaft, which is well defined and slightly more dense than normal. The bones of the forearm are atrophic, otherwise normal. There is swelling of soft tissues of the upper part of the arm.

From the x-ray film alone, scurvy, rickets, and probably syphilis can be ruled out because the lesion involves only one bone. Trauma rarely makes such marked changes without definite evidence of a fracture, which is lacking here. The lesion is rather old, as the new bone is fairly dense, and also the shaft is dense, which suggests that it is sequestrated. Two points are uncommon for osteomyelitis: one, the very young age of the patient; the other, the sequestration of an entire shaft without irregular erosion of the shaft.

The history was that, at three months of age, the child had whooping cough followed by a left-sided pneumonia. While recovering from the pneumonia, the right arm became swollen and tender, and after two days was incised near the shoulder.

The swelling subsided and a discharging sinus persisted. After ten weeks there was a recurrence of swelling and inflammation and increased discharge, at which time the child entered the hospital.

Combining this history with the x-ray findings the diagnosis of osteomyelitis is practically certain, and the operation confirmed this diagnosis. The sequestrated shaft was removed *en masse* through an incision in the involucrum. A satisfactory new shaft formed later.

Case 2. The x-ray film of this year-old Lithuanian child shows periosteal new bone the entire length of both femurs, more markedly elevated in the upper half of each shaft, where it rises to a maximum of two centimeters. Subepiphyseal bone absorption has led to displacement of the shaft at the upper end of both femurs. All of these changes are a little more marked on the right side and there is also marked swelling of the soft tissues of the right leg. The tibias and fibulas show these changes in a less marked degree, accompanied by slight thickening of the metaphyseal margins. The distal epiphysis of each radius and ulna is dense, and there is no bone absorption, or periosteal new bone along the shafts.

These x-ray findings strongly indicate scurvy, because of their character and their multiplicity, and the age of the patient. It is a severe scurvy, complicated by fractures, and with large subperiosteal hemorrhages which now show calcification. Yet why is there swelling of the right leg? Had this leg only been rayed, the findings would closely simulate the osteomyelitis of the last case. Indeed, when the child came to the dispensary, the clinical findings were entirely referable to the right femur, and very suggestive of osteomyelitis.

The right leg was swollen, red hot, and painful. It did not pit on pressure. The other extremities were not swollen, nor discolored, and did not seem to be painful. The child's temperature was 102.4 degrees.

The history revealed that three months previously, while teething, the baby had a severe diarrhea, with six to ten greenish stools per day. Four weeks later, after being chilled while out-of-doors, the baby's legs, thighs, right arm, and areas under the eyes became edematous. The swelling, except that of the right leg, had disappeared two weeks before coming to the clinic.

The mother refused to hospitalize the child. Dietary measures, including orange juice, were prescribed. The mother did not bring the child to the clinic again. A Social Service worker found that the child died at home two weeks after the visit to the Clinic.

Was this *only* scurvy? If so, why had the swelling remained in the right leg, or was there really an osteomyelitis in this leg superimposed on a scurvy?

Case 3. The films of this 18-months-old white girl show elevation of periosteal new bone for from 2 to 7 mm. above the entire shaft of the right ulna and the upper third of the left ulna. There is a homogeneous calcification between the shaft and the periosteal margin. The shaft is distinctly visible and unchanged. In addition, five bones in the hands and two in the feet show irregular destruction of the shaft and heavy irregular periosteal new bone, with flask-like swelling of soft tissues, all of which, when associated, are characteristic of tuberculous dactylitis.

The tuberculous dactylitis at once suggests that the lesions of the ulnas are also tuberculous, although the changes described in the ulnas are rare in tuberculosis, and especially in children. The periosteal reaction of syphilis is suggested, although unlikely since other bones are not involved. Rickets and scurvy are ruled out because of the absence of epiphyseal involvement. Subperiosteal hemorrhage without fracture, or osteomyelitis without involvement of the shaft, are illogical, especially since such lesions almost never involve two bones in about the same degree, such as occurs in this patient.

This child, one of twins, weighed six and one-half pounds at birth, and seemed normal. It was breast-fed for three months, and afterward with various milk mixtures

and infant's foods. There were occasional attacks of diarrhea, but no other illnesses until about four months before entering the hospital. Then, at 14 months of age, there occurred swelling in multiple areas of the hands, and in both ankles, corresponding to the sites of the bone lesions shown later on the films. The swollen members gradually enlarged to one or two inches in diameter, became red, tender, slightly fluctuant although not particularly painful. From several, a sero-purulent discharge exuded. At this stage the child entered the hospital. Although fairly well nourished, the child was fretful and looked ill. There was no fever. The von Pirquet test was strongly positive.

Fig. 3. Case 3. Film of upper extremities shows elevation of periosteal new bone extending from 2 to 7 cm. from the entire shaft of the right ulna and the upper third of the left ulna. Five bones in the hands show irregular density of the shaft and irregular periosteal new bone, with flask-like swelling of the soft tissues, characteristic for tuberculous dactylitis. Two bones in the foot were similarly involved.

Nothing in the child's history or physical findings suggested the bone lesions which were found in the ulnas by x-ray examination.

The swollen areas of the hands and ankles were incised and a considerable amount of grayish-yellow, "tuberculous

Fig. 4. Case 4. Films show a fusiform periosteal elevation of 5 mm. (maximum height) over the lower half of each humerus and the upper half of each ulna, and the entire metacarpal of the left index finger. There is a laminated, fairly dense calcification between the shafts and the periosteal margins. The shafts are distinctly visible and unchanged. The mid-part of the right tibia was similarly involved.

Fig. 5-*A*. Case 5. Anteroposterior and lateral views of the right forearm show periosteal elevation of the entire right ulna.

type" of pus and several small bone fragments were removed. Cultures showed a very scanty growth of pyogenic organisms, none of tubercle bacilli. Microscopic sections showed tuberculous tissue, with many giant cells. This evidence confirmed the clinical and x-ray diagnosis of multiple tuberculous dactylitis, and, because of this evidence, the fusiform periosteal elevation in both ulnas was believed to be tuberculous in nature, although not examined microscopically.

Case 4. This is a white child, four and a half years old. Films show a fusiform periosteal elevation of 5 mm. maximum height over the lower half of each humerus and upper half of each ulna and the mid-part of the right tibia. There is a laminated, fairly dense calcification between the shaft and the periosteal margin, while the shaft itself is distinctly visible and unchanged. The entire metacarpal of the left index finger is similarly involved. The right tarsal scaphoid is small, dense, and irregular—a characteristic Köhler's disease. The unaffected portions of the involved bones, as well as all other bones of the extremities, are normal.

The laminated periosteal thickening of one metacarpal and five other long bones is very suggestive of a syphilitic lesion. Involvement of about half of a shaft, with the other half normal, is not uncommon in the syphilis of children, especially in the very young. This child is rather old for this type of lesion, still it *might* be a lues tarda. Rickets and scurvy can be ruled out by the absence of epiphyseal line changes, and osteomyelitis because of the uniformity of the involvement in several bones simultaneously. In view of the peculiar manifestation of tuberculosis in the previous case, the possibility that these lesions might also be tuberculous was not forgotten, but could not be proved from the x-ray examination alone.

Fig. 5-*B*. Case 5. Anteroposterior and lateral views of the right lower extremity show periosteal elevation in the mid-part of the fibula and in the right fifth metatarsal.

The new bone beneath the elevated periosteum is loculated, especially that of the ulna. The bone shafts, although slightly atrophic, are fairly well shown through the periosteal new bone. There is a little associated swelling of soft parts, especially over the ulna. All other bones are normal.

This child, a mongolian idiot, with a cleft palate, came to the hospital because of swollen glands of a year and a half duration, and recent convulsive attacks, with occasional loss of consciousness. The glands of the neck had become enlarged three months after the breaking of a tooth, and had remained large ever since. One gland had become red and sore, was incised, and had drained pus for six months. On examination of this child, the cervicals, inguinals, and epitrochlears were all palpable and ranged in size from bird shot to that of a pea. Healed keloid-like scars were present in each submandibular region. Marked thickening of the arms and legs could be palpated, especially of the humeri and the left tibia.

The von Pirquet was strongly positive; basal rate was −14; leukocyte counts varied from three to eight thousand.

A biopsy of a cervical gland and the right tibia was done. The cultures and guinea pigs were reported negative for tuberculosis. The microscopic sections of both the gland and the tibia showed findings which were considered to be tuberculous. It was believed, therefore, that all these bone lesions were tuberculous in nature.

Tuberculous osteomyelitis of the long bones in children is rare, and I am fortunate to be able to present these two cases.

Case 5. This is a colored child, 18 months old. Films show periosteal elevation of the entire ulna, the middle of the right fibula, and the entire right fifth metatarsal. The new bone beneath the elevated periosteum is loculated, especially that of the ulna. The bone shafts, although slightly atrophic, are fairly well shown through the periosteal new bone. There is a little associated swelling of soft parts, especially over the ulna. All other bones are normal.

Osteomyelitis may be multiple, and should be considered. Against it is the fact that the lesions are all in practically the same stage, and also that one lesion is in the middle of a shaft away from the entrance site of the nutrient vessel. The lesion in the foot strongly suggests a tuberculous dactylitis, and, therefore, the other two may also be on a tuberculous basis. Syphilis is sometimes localized, or focal, in its manifestation, but rarely is there so pronounced a local lesion involving three areas, and not involving other bones also. The associated swelling of the soft tissues could fit either with osteomyelitis or tuberculosis, and perhaps also with syphilis. Absence of epiphyseal changes rules out rickets and scurvy. Bone cysts are rarely multiple. Fibrocystic disease or myeloma usually involves the shaft rather than the periosteum. Periosteal tumors are rare in children and almost never multiple.

The history reveals that this child was seen in the Central Free Dispensary when one month of age, and seemed normal except for a palpable right epitrochlear gland. The Wassermann test was then

negative. The child was next seen when 11 months of age, at which time a fluctuating swelling of two or three weeks' duration was present over the right forearm, with smaller swellings near the right knee and on the right foot. The swollen areas were moderately tender, not red, and did not seem acute. The Wassermann test at this time was strongly positive. Antisyphilitic treatment was instituted, and continued for four months. Films taken after three months of treatment show a very slight increase in the bone density of the involved areas; otherwise no change. The soft tissues, however, had ulcerated in the areas of previous swelling. The von Pirquet test was negative at this time and the Wassermann again strongly positive. The mother's Wassermann was also positive.

From all of this evidence, both clinical and from x-ray films, a congenital syphilis, with secondary osteomyelitic infection, was considered as the most probable diagnosis, and removal of the sequestrum in the ulna was advised. This was not carried out, however, as the parents were leaving for the South and the child did not remain for further observation and treatment.

SUMMARY

In conclusion, I wish to emphasize that x-ray findings which are strikingly similar, may, in reality, be due to widely different clinical conditions, as proved by clinical and pathologic evidence.

An interpretation, based on x-ray findings alone, may lead to a wrong diagnosis, especially in unusual cases, if the clinical history and the pathologic findings are not considered, and even after a most careful study one may still be in doubt, as in two of the cases here reported.

Unusual change in one bone should stimulate the study of other bones of that patient.

My plea is for the close co-operation of the clinician and the roentgenologist for the good of the patient.

WHAT KIND OF TUBE DID RÖNTGEN USE WHEN HE DISCOVERED THE X-RAY?[1]

By OTTO GLASSER, PH.D., Cleveland Clinic Foundation, *Cleveland, Ohio*

I FEEL that we should not let this great meeting at which we heard so many excellent reports on the use of the roentgen rays go by without calling attention to the fact that we celebrate this year, the fortieth anniversay of the discovery of the x-ray or roentgen ray. Forty years have passed since Wilhelm Conrad Röntgen, Professor of Physics at the University of Würzburg, saw a strange phenomenon—the bright fluorescence of some barium platinocyanide crystals near an excited evacuated tube. He pursued the study of this effect in a most masterly and thorough manner, and discovered it to be due to a "new kind of rays," which he called the "x-rays."

Many stories and fables have been woven around this famous discovery, some of which I have attempted to unravel in my book on the life of Röntgen (1). Even now, forty years later, discussions about the details of the discovery continue. Only recently, a discussion was again begun about the type of tube which Röntgen used when he made the discovery. Several articles have appeared in the last few months in German journals attempting to prove that Röntgen's work with a Lenard cathode-ray tube and not with a Hittorf-Crookes tube, led to the discovery. The titles of three of the communications are: "On the History of the Discovery of the Roentgen Rays," by J. Stark (2), President of the Physikalisch-Technische Reichsanstalt; "On the Roentgen Rays Emitted from the Platinum Seal of a Lenard Window Tube," by F. Schmidt (3), Professor of Physics at Lenard's Heidelberg Institute, and "On the Discovery of the Rays Named after Röntgen," by O. Rössler (4), a Baden-Baden pharmacist and former co-student of Lenard.

The tendency in these articles is to credit Lenard, the famous Heidelberg physicist.[2] This is perhaps best summarized by Rössler in his short article in the Münchener Medizinische Wochenschrift" in which he states: "In 1895, Röntgen became very much interested in Lenard's work and experiments, and asked Lenard to assist him in the repetition of these experiments. Lenard had built his first tube himself but then had ordered an improved tube from a shop for physical instruments. Since this tube was expensive, and since Lenard had only a very moderate income, he could not acquire it. He, therefore, wrote to Röntgen and asked him to buy this instrument with which he could make further studies. Röntgen did so and was able to find with this tube those rays which have become so useful in practical medicine." These statements which link the name of Lenard with that of Röntgen in the history of the discovery unfortunately come at a rather late date. They should have been proposed while Röntgen was still alive. However, they recall some remarks which Lenard made on various occasions in past years.

Phillip Lenard, who is now Emeritus Professor of Physics at the University of Heidelberg, is one of the few surviving predecessors of Röntgen in the genealogy of x-rays (5). There is no doubt but that Lenard's outstanding investigations on the various properties of cathode rays formed the most significant basis for the discovery of the roentgen rays, a fact which Röntgen mentioned in his first communication, by speaking of Lenard's "wonderful experiments."

When I began to collect the material for my historical studies on the roentgen rays, I wrote to many of the early pioneers and,

[1] Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, in Detroit, Dec. 2–6, 1935.

[2] A rather mysterious article with similar suggestions was written by one Erhard Grieder and appeared in the March 1, 1935, issue of the "Zürcher Illustrierte Zeitung." It is, however, so full of untruthful statements that it is not worth while to discuss it here.

among them, Lenard. At various times, Lenard very cordially gave valuable information regarding the circumstances surrounding the discovery of the roentgen rays, but in his letters, as well as in his printed communications on the subject, he frequently hinted at some as yet unknown connection between the discovery proper and the part which he played in it. On Aug. 18, 1929, he wrote, for instance, in a personal communication: "There is no doubt that the road to the discovery led over my researches. At that time I was prevented by external circumstances from pursuing to my satisfaction in every direction the great number of new phenomena which appeared in my studies on cathode rays. But in my opinion, this is not yet the proper time to express myself more thoroughly on the subject than I did in my Nobel prize lecture (6). That would be only biographical anyway and what has already been said must suffice for the judicious. With this I believe that I have done everything that the history of science can expect of me on this point at this particular time." In a previous publication (7), during a controversy about the discovery, Lenard also intimated that perhaps more data in regard to the discovery might be produced at a later date.

Both Stark (2) and Schmidt (3) in their recent statements may now have furnished the information to which Lenard referred many years ago. Stark (2) presents copies of the original correspondence in 1895 between Lenard and Röntgen regarding the acquisition of the Lenard tube from the glass technician, Müller-Unkel, then analyzes the circumstances surrounding the discovery and comes to the definite conclusion that Röntgen must have used the Lenard tube when he made his discovery. Stark then enumerates three important experimental conditions which favored Röntgen rather than Lenard in preparing the ground for the discovery: (1) Röntgen had obtained the best Lenard tube available; (2) Röntgen surrounded his tube with black cardboard, which reduced the intensity of the then unknown x-rays much less than the zinc box which Lenard always used to shield his tube; (3) Röntgen used in his observations on cathode rays, a barium platinocyanide screen, which responds much more to x-rays than the pentadecylparatolylketone screen which Lenard used. Thus, Stark concludes that under the given experimental conditions, it was inevitable that Röntgen should make his discovery.

J. Schmidt's (3) paper, which appeared in the "Physikalische Zeitschrift," immediately follows Stark's publication and describes his successful attempts to demonstrate the existence of x-rays near the platinum seal window of a Lenard tube, using an exact replica of the one which Röntgen bought from the firm of Müller-Unkel prior to his discovery. This proof also includes a study of the efficiency of various fluorescent screens. Schmidt explains again that Lenard, in his investigations of cathode rays, observed certain strange phenomena, the investigation of which he postponed, however, in order to study more thoroughly the primary objects of his interest, the cathode rays; thus Lenard missed the interpretation that these strange phenomena were due to a hitherto undiscovered kind of rays. Both Schmidt and Rössler (4) conclude their articles in a vein similar to that of Stark's article.

On the other hand, the view that Röntgen used a Hittorf-Crookes tube at the time of the discovery has been and is held by many. I proposed this view in my book on Röntgen (1) after having closely examined several sources for this report. One of the most reliable of these sources comes from L. Zehnder, who was a good friend of Röntgen and his assistant and co-worker for many years. Zehnder definitely states in his recent book (8), "Letters of Röntgen and Zehnder," that Röntgen used the Hittorf tube when he discovered the x-ray. Zehnder's own words are: "When I saw Röntgen after the discovery, he told me that he discovered the rays with the Hittorf tube and not with the Lenard tube. Friends of Lenard are spreading the myth that Lenard was the real discoverer of the roentgen rays, and they believe that Röntg

gen, working with the Lenard tube, did not discover anything essentially new, even though Röntgen in his famous original communication (9) on the x-ray spoke first of the Hittorf tube and mentioned the Lenard tube only in second place. One must always remember that Röntgen was extremely careful in his scientific statements."

Are these two points of view in regard to the tube used at the time of the discovery irreconcilable? I believe that they are not. A careful analysis of the situation would seem to present the following picture: Röntgen himself stated (1) that he became interested in the problem of cathode rays from vacuum tubes as studied by Hertz and Lenard, and that in October, 1895, he began to make researches of his own. There seems to be little doubt but that in these early experiments he used the Lenard tube described above. It is probable that in investigating the cathode rays emitted from this tube with his barium platinocyanide screen, he found that he obtained an effect at distances and angles greater than those described by Lenard. This made him look for similar effects on windowless tubes which, according to previous experience, did not permit the cathode rays to penetrate the wall and reach the outside air. Such a windowless tube was the Hittorf or Crookes tube. Still, he observed effects on his screen also with these tubes. Since the properties of cathode rays known up to that time did not account for the effect, Röntgen realized that he had to deal with either a type of cathode rays of hitherto unknown penetrability, or with a new kind of ray. His thorough researches which proved that they were the latter are well known and need not be repeated here.

The new material brought forth by Stark and Schmidt is valuable since it gives a better insight into some phases of the actual discovery. As far as their conclusions are concerned, I feel that they have to be modified to the degree explained above. Whichever of the two tubes was actually used in the first crucial observation which made Röntgen feel that he had something new, really does not matter. The discovery itself is one of the greatest of all times and the discoverer has earned immortal fame.

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DILATATION OF THE PULMONARY ARTERY OF CONGENITAL ORIGIN

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A MODERATE degree of increase in the diameter of the first portion of the pulmonary artery occurs in numerous conditions, although it is not mentioned frequently in reports of roentgen examinations. However, communications regarding marked generalized broadening of the artery or aneurysmal dilatations are infrequent in the literature and actual aneurysms of this vessel are very rare. Little attention has been paid by American roentgenologists to the radiologic criteria for diagnosis of abnormalities affecting this structure. In one patient coming under our observation, particular interest was attached to his condition because of the marked degree of dilatation of not only the main stem but of the branches, the lack of recognition of the underlying congenital defects at previous examinations, the clinical course during a period of observation, and the autopsy findings. In another, aneurysms of the pulmonary artery of congenital origin were found at autopsy after repeated examinations by various consultants had failed to yield the correct diagnosis.

CASE REPORTS

Case 1. H. Y., white male, aged 38 years, came for a roentgen film study of the chest on account of the clinical findings by one of us (W. P. M.) of slight cyanosis, cardiac enlargement, and a presystolic murmur, heard best at the left nipple. His primary complaint was intermittent nasal obstruction which had begun in early life, but also he had long been bothered by coldness and discomfort in the feet. Although throughout his childhood he had been rather frail and had some dyspnea on exertion, he engaged in fairly strenuous physical activities in play and farm work. Upon college entrance he was barred by the university physician from college athletics because of "heart disease," a diagnosis later confirmed by other physicians, but he had regarded neither this nor the diagnosis of pulmonary tuberculosis which was made when he was 26 as of serious import. The history was otherwise irrelevant.

Physical Findings.—The lips, nails, and cheeks were slightly cyanotic. A turgescent rhinitis was present. The chest measured 36 inches on inspiration, 33.5 inches on expiration. The heart was enlarged, with the apex impulse at the seventh interspace in the axillary line. There was a snappy pulmonic second sound, plus a presystolic murmur heard best at the nipple. Auscultation and percussion of the chest and the other physical findings were of no particular significance.

The blood pressure was 140/80. Urine examination was negative. Hemoglobin, 100 per cent; red blood cells, 6,112,000; white blood cells, 9,900, with a distribution of 80 per cent neutrophiles, 14 per cent lymphocytes, 4 per cent eosinophiles, and 2 per cent monocytes.

Roentgen study revealed a globular heart, greatly increased to the right and left, with much broadening of the pulmonary trunk markings (Fig. 1).

Three years later the man returned on account of pain of three weeks' duration, located in the region of the anterior ends of the left second and third ribs, aggravated by cough or deep inspiration. The heart as studied radiographically was a little increased in size over that found in the former examination.

He was seen again eight months later, when there were clinical and roentgen evidences of lobar pneumonia in the upper lung-field on each side. Fluoroscopically,

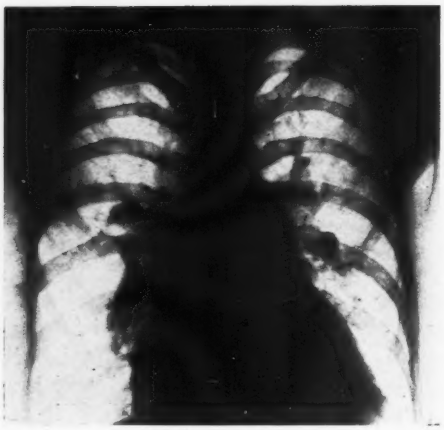

Fig. 1. Case 1.

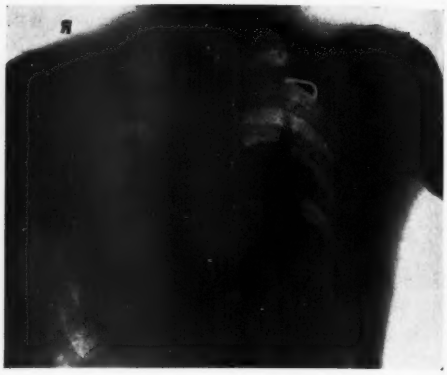

Fig. 2. Case 2.

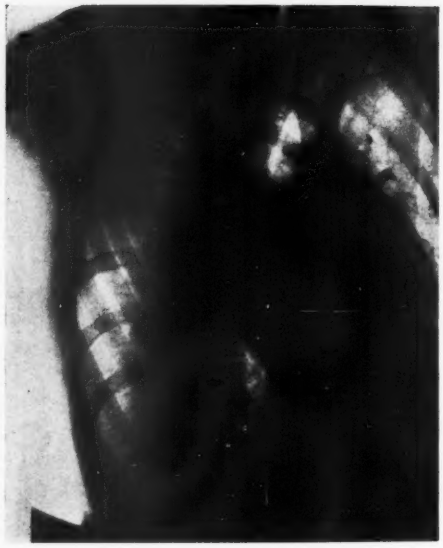

Fig. 3. Case 2. Right anterior oblique projection.

a striking appearance was presented by the combination of the two conditions, with a definitely expansile pulsation of the large vascular structures seen in optical section in the pulmonary parenchyma.

Radiographic study nine months later gave the same findings as at the first study 52 months previously. Five months after this fourth and last roentgen examination, he re-entered the hospital with symptoms of infection in each lower lung-field. His endurance had been below par for the preceding year. The cardiac apex extended 3 cm. to the left of the midclavicular line. Exitus occurred suddenly in an attack of extreme cyanosis seven days after the onset of acute symptoms. The clinical and roentgen diagnoses of the condition here considered were congenital dilatation of the pulmonary artery arising on the basis of a congenital cardiac defect.

Necropsy, performed by Dr. Wemple Dodds, revealed a very greatly enlarged heart weighing 663 grams, which extended 8 cm. to the right of the median line and 12 cm. to the left, being greatly hypertrophied throughout but especially in the right chambers. There was congenital absence of the interauricular septum, making the heart trilocular. The mitral valve was slightly stenosed, with sclerotic changes. The aortic, tricuspid, and pulmonic valves were normal. Atheromatous changes were of moderate degree in the aorta, being much more marked in the pulmonary artery and its branches, with numerous atheromatous ulcers in the main trunk. The pulmonary artery was congenitally dilated throughout, the main trunk being 5 cm. in diameter. Antemortem thrombosis was present in all the arteries of the left lower lobe. The pulmonary veins were markedly dilated. Lung changes, secondarily of congenital origin, where chronic emphysema and chronic passive congestion with bilateral chronic interstitial pneumonia. A more

recent pneumonic process existed in each lower lobe, that in the left surrounding a bronchiectatic abscess. The only obvious immediate cause of death was the pulmonary thrombosis.

Case 2. P. W., white male, aged 30 years, was brought by his father, a physician, for consideration of roentgen therapy on account of a mediastinal tumor. He had always had "lung trouble." His cough was very annoying and there was much dyspnea and substernal pain. Numerous physicians had been consulted, including those at a large general clinic. The first roentgen study of the chest had been made two years previously, when a large mediastinal tumor was found, the nature of which had never been determined.

Radiographs of the chest were made at this time (Figs. 2 and 3); the previous radiographs were not available for comparison. As studied in the postero-anterior projection, there was seen a much enlarged heart shadow, the increase being chiefly to the left. Fusing with the upper part of the cardiac shadow and extending outward into the left pulmonary field was a rather rounded, non-pulsating mass. Extending outward into the right pulmonary field, two-thirds the width of the right chest, was another, larger mass, also without expansile pulsation. The aortic arch was not demonstrable in this projection. The trunk markings in the pulmonary fields were increased moderately over the normal, more so on the left than on the right. The trachea was displaced appreciably to the right, at and just above the level of the bifurcation.

Study in the right anterior oblique plane gave evidence of a considerable degree of anteroposterior increase in the cardiac diameter. The normal outlines of the upper portion of the heart and the aortic arch could not be distinguished. In this and in the left lateral view there was evidence of a large tumor mass superimposed upon the structures in this vicinity, with a rounded superior margin. Extending to the right posterior from this tumor mass was a projection of large size which reached from the level of the sixth dorsal vertebral body to that of the tenth.

The patient's condition steadily grew worse, and Dr. Bond was consulted. All medical therapy failing, exitus occurred fifteen months after our examination.

Autopsy was performed by Dr. H. M. Banks, to whom we are indebted for the necropsy report.[1] The pulmonary artery was found to be greatly distended, with a diameter of 5 cm. in its main portion. There were fusiform dilatations of the right and left branches just beyond the bifurcation, extending well out into the lungs, that on the right being 8 cm. in diameter, and on the left, 6 centimeters. The walls were markedly thinned and the lumen filled with a canalized, lamellated clot. Much dilatation of the pulmonary veins had resulted from pressure by the masses. No evidence of congenital defect of the heart was found but it was enlarged to about three times the normal size, the increase being in the right chambers. The valves were normal. Much parenchymatous fibrosis and sclerotic obliterative arterial changes were found in the lungs.

Contributions in the literature have dealt mostly with changes in the main stem of the pulmonary artery, there being relatively few comments upon the roentgenologic demonstration of enlarged distal branches. The literature upon aneurysm of the pulmonary artery has been extensively reviewed by Henschen, Posselt, and, more recently, by D'Aunoy and von Haam, who have analyzed most of the reported cases as to age, sex, anatomic findings, etiology, and associated abnormalities in the circulatory system. D'Aunoy and von Haam account for a total of 87 instances reported with autopsy findings since 1833 and give an excellent bibliography upon the subject. Since their article appeared, Joules, Scott, and Holst have reported upon the condition. They have omitted reference to the reports of Balaban and Pokidoff, Dietrich, Posselt, Kranz,

[1] The complete autopsy findings will be reported elsewhere by Dr. Banks.

and Hochsinger. Kranz discusses a diagnosis of aneurysm of this vessel made from clinical and roentgen studies but without autopsy, and considers the differential diagnosis.

References bearing upon general widening of the lumen of the pulmonary artery are plentiful but few of these bear upon the roentgen appearance. Posselt reviews the general literature up to 1909. Assmann discusses the condition from both clinical and roentgen standpoints. Zeidler and Jaffé have described four instances of a lesion similar to the first herein reported, three of these having been observed during life. Posselt and Vierordt state that at the autopsy table a moderate dilatation is not a rare finding. Roesler reports a case of interatrial septal defect and gives an extensive analysis of the literature, not including, however, the cases of complete absence of the septum.

Etiology.—Assmann has listed the causative factors of increase in the pulmonary bow, the first part of the pulmonary artery as seen on the roentgen film in the anteroposterior projection, as follows:

(*a*) *Acquired:*
1. Aneurysm of the pulmonary artery.
2. Perforation of aneurysm of the aorta into the pulmonary artery.
3. Pulmonary insufficiency resulting from endocarditis.
4. Deformity from scar-contracture developing in scirrhosis of adjacent lung tissues.
5. Stasis in pulmonary circulation from various causes, most frequently from high-grade valvular incompetency and particularly from mitral stenosis.
6. Sclerosis of pulmonary artery.

(*b*) *Congenital:*
1. Solitary, single anomaly. (Asymmetrical division of truncus arteriosus communis.)
2. Open ductus Botalli.
3. Pulmonary stenosis (an exceptional cause).
4. Defect of ventricular septum.
5. Defect of auricular septum.
6. Transposition of vessels plus a ventricle septum defect.
7. Tricuspid insufficiency.
8. Sclerosis of branches of the pulmonary artery.
9. Stenosis of isthmus aortæ below opening of ductus.

Prominence of the pulmonary bow is frequently the only roentgenographic sign of a congenital cardiac lesion and is present as a rule in adults having such a lesion. It is not usually present in the early months of such a patient's life (8), as it requires a period of time to develop dilatation of the pulmonary artery as a consequence of prolonged exposure to ventricular and aortic backpressure. Except in the cases with asymmetrical division of the truncus arteriosus communis, such abnormal pressure is the common causative factor, resulting usually from: (1) communication between pulmonary artery and aorta; (2) communication between the right and left ventricle, or (3) stasis in pulmonary circulation from other causes (2). Our first case had a congenital cyanosis and widening of the pulmonary artery. The former has been shown to be due usually to pulmonary stenosis, but such stenosis is only exceptionally associated with widening of the pulmonary artery (2), according to the German teaching. Vaquez and Bordet, however, take exactly the opposite view on the latter point (9).

D'Aunoy and von Haam discuss the evidence adduced by various writers which tends to show that local damage to vessel wall and increased blood pressure are important causative factors of aneurysm of the pulmonary artery. The former may result from long-continued impingement of a jet of blood upon the wall of the artery immediately distal to a stenosed pulmonary valve or opposite the opening of the ductus arteriosus into the pulmonary. They emphasize that sclerosis and syphilis seem to play a less important part in aneurysm here than in the aorta, although the former has been re-

peatedly mentioned as a factor. Increase in pressure in the pulmonary artery can result from a patent ductus, a congenital cardiac lesion such as a septal defect, or a mitral lesion with its resulting back-pressure. Peck considers approximately 25 per cent of reported cases to have been syphilitic in origin. Trauma has been considered the cause in several (5 and 14), and congenital defects in the wall of the artery have been rated as important by Costa. However, congenital anomalies of the heart or imperfect closure of the ductus arteriosus are acknowledged to stand out among the frequent findings.

Diffuse, generalized broadening of the pulmonary artery may have as its cause one of the factors quoted above from Assmann, or any of those conditions associated with even a temporary increase in pulmonary blood pressure, particularly a mitral defect. Stasis in the vessels from some other cause, such as pulmonary sclerosis, marked scoliosis, bronchial asthma or emphysema, may also cause it.

Local, or at times a general, widening of the arterial branches can also occur as a result of scar-contracture of adjacent tissues, as in tuberculosis or chronic pneumonia (5).

Age and Sex.—Diffuse broadening of the general pulmonary arterial tree may, of course, occur at any age, as a result of any of the conditions enumerated in which there is a material increase in the back-pressure in the pulmonary circulation. Patients with congenital defects of the type mentioned are naturally more likely to exhibit this change at an earlier age than those developing such increased back-pressure from acquired lesions. Aneurysms of the first part of the pulmonary artery have been reported in patients of all age groups. It has been observed that in young persons aneurysms of the pulmonary artery are found more frequently than are aneurysms of the aorta. Some 38 to 50 per cent of the reported cases of aneurysm of this type have been found in persons under thirty years of age (7 and 19). In the majority of patients under thirty years of age, these aneurysms are coincident with malformations. The small aneurysms which are not uncommonly found in pulmonary tuberculous cavities may be found at any age in cases in which such cavitation occurs. Males and females show the same frequency of involvement by this type of aneurysm. There is a prevalence of the female over the male sex in the proportion of 3:2 in the occurrence of interatrial septal defects, which are a frequent cause of dilatation of the pulmonary artery (20).

Morphology.—The trunk of the artery has been the site of the aneurysm in some 85 per cent, the pulmonary arterial branches in 15 per cent (4). Usually the aneurysm formations are single but may be multiple as in cavitating tuberculosis or bronchiectasis. The shape is ordinarily fusiform but may be sacculated. These aneurysms may become very large. It has been noted that the media and intima are quickly destroyed by trauma resulting from the causative factors which have already been mentioned. The lamellated clot which is usually present may occlude the entire lumen. The histologic appearance does not differ greatly from that usually found in aneurysm of the aorta (5). Endarteritis, thrombosis, and atheromatous changes involving the pulmonary arteries, as found in our cases, have often been found (5, 19, and 20). Peck, who has described the syphilitic lesions which have been found in the pulmonary artery, notes that in addition to the type resembling syphilitic aortitis, there is found a more common type with small miliary circumscribed gummas in the media or intima. He considers that this more common second type does not produce a true aneurysm. Congenital defects of the wall have already been mentioned.

The associated changes have already been noted in consideration of the etiologic factors. Prominent among these are the congenital malformations, particularly in association with the diffuse generalized broadening of the arterial tree. As might logically be expected in these, the right ventricle tends to be greatly hypertrophied

as a result of the stress against which it must necessarily act; also, the left ventricle is small. The auricles may form one large chamber, as noted in our first case. The aorta is small (20). As in our first patient, there tends to be marked infarction of the lung supplied by the involved branch of the pulmonary artery in cases of aneurysm.

Clinical Symptoms.—Most examiners, we believe, would have been impressed by the asymptomatic cyanosis in Case 1, and would have marvelled at the patient's ability to carry on his work which, as a matter of fact, entailed considerable physical exertion. The case strikingly demonstrates the heart's ability to compensate for both intrinsic and extrinsic defects, and brings out the relationship between asymptomatic cyanosis and congenital heart lesions. During the last two or three years of this patient's life he was at times slightly conscious of shortness of breath, but insisted that it was due to nasal obstruction.

The clinical symptoms of general dilatation of the pulmonary artery are largely those of the causative factor, as indicated in the paragraph on etiology, plus those arising from circulatory stasis in the pulmonary circulation. Assmann has discussed these aspects in some detail; he notes that the physical findings as to heart and blood vessels were not the same in character or degree in various cases. Of his 15 cases personally observed that had increase in the pulmonary bow, all were cases of congenital heart disease, mostly in adults and almost without exception in well developed patients. Cyanosis and finger changes were lacking in all cases with one exception; however, there was in most a slight bluish-red discoloration of the lips and cheeks. As would be expected with increased pressure in the pulmonary circulation, there is clinical and electrocardiographic evidence of right ventricular hypertrophy. Less frequently there are also dilatation and hypertrophy of the left ventricle.

Much the same symptoms may exist in aneurysm of the pulmonary artery, since this may often arise from the same etiologic factors as are found causative of generalized pulmonary artery increase. Pain in the cardiac area may be very marked, as in our second case, and cough may be an annoying symptom. Dyspnea may be striking (1). The symptoms and clinical findings have been discussed by Kranz and Roesler. There may be a visible protuberance on the chest wall over the area of the pulmonary aneurysm, with or without visible pulsation in the second and third interspaces. A bruit may be evident. Dullness is present in the second and third interspaces at the left of the sternum. A venous stasis may be found in the neck.

Radiologic Criteria in Diagnosis.—It seems strange that roentgen literature itself has but few references to the radiographic appearance of dilatation of the pulmonary artery and its differential diagnosis. This has resulted in many erroneous diagnoses (20), the most common of which have been tumor and tuberculosis.

Variations from the roentgen normal in this condition, dependent solely upon the dilatation of the pulmonary artery itself, consist of the following: an increase in the pulmonary bow; a small aortic knob (2, 20, and 22); broadening of the hilum shadows; a degree of broadening of the pulmonary arterial tree which will vary according to the etiologic factors and their duration; an enlargement of the cardiac outline. The right anterior oblique position is better adapted to the differentiation of the pulmonary bow increase than is the postero-anterior. Expansile pulsation in this part, as in the hilum portions, may or may not be present, depending upon the presence of lamellated clot. Rosenfeld, who was one of the first to study fluoroscopically an aneurysm of the pulmonary, called attention to the value of the Valsalva test, referring to increase in the pulmonary bow on forced inspiration with the glottis closed. In a generalized dilatation the accentuation of the vascular markings in the pulmonary field may be a striking feature, as in Case 1, in which instance there

was a marked expansile pulsation evident in the arteries. Pezzi has termed this expansile pulsation "the hilum dance." The appearance of such dilatation may be very confusing if a pneumonic change is also present, as was found in Case 1. The tendency to thrombosis may add infarction to the radiographic picture. If there is increased pulse pressure in the pulmonary circulation, there may be sufficient expansion of the lung structure with each pulse-beat to produce a "dance of the diaphragm" (27), superimposed upon the respiratory movements.

Absence of the aortic knob at the left may occur in great enlargement of the pulmonary artery from any cause, as in marked mitral stenosis or in coarctation of the aorta, and in instances of right-sided aortic arch (20).

The cardiac outline may be of the congenital or mitral type (27). In the instances of congenital origin, it is conditioned in chief part by the great hypertrophy of the right ventricle, although the increase may be mostly to the left of the mid-line.

The differential diagnosis of dilatations of the first part of the pulmonary artery is not difficult in those patients exhibiting it in minor degree, this being a not uncommon finding in conditions of pulmonary circulatory stasis. If the dilatation is marked and there is a lamellated blood clot, differentiation from a mediastinal tumor may be somewhat difficult if the condition is not kept in mind as a possibility. In one instance thus erroneously diagnosed the patient died from hemorrhage after incision of the mass (30). Films made in the right anterior oblique projection are particularly helpful here, in which view an aortic aneurysm or the usual mediastinal tumor is projected more medially. At the hilum, as already mentioned, the vascular dilatation has been mistaken for tuberculosis, tumor, or adenopathy. The appearance of chronic bronchitis is quite different from that of diffuse arterial dilatation. Differentiation from aneurysm of the ductus arteriosus need rarely be made, as Traum has reported apparently the only case on record.

SUMMARY

Two cases of unusual broadening of the pulmonary artery are described, one a diffuse generalized dilatation of the pulmonary artery, and the second an aneurysm of the main stem and right and left branches, each arising as a result of congenital abnormality. Each was studied at autopsy, the diagnosis in Case 1 being made from the radiologic findings during life, and the second only at autopsy notwithstanding numerous consultations. Case 1 presents unusual features in that there was a marked diffuse dilatation of the pulmonary arterial tree of a type which in less marked degree is well known to pathologists but which has been little discussed in roentgen literature, arising on the basis of a congenital cardiac defect, and absence of the interauricular septum. This case was observed over a period of almost five years. Case 2, an aneurysm of the pulmonary artery undiagnosed until autopsy, apparently had its origin in a congenitally weak arterial wall. The literature and radiologic findings are discussed.

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THE USE OF GEIGER-MÜLLER COUNTERS FOR LOCATING RADIUM AND FOR MEASURING GAMMA-RAY INTENSITIES

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THE development of Geiger-Müller counters to a state of good reliability has provided a new order of sensitivity and facility with which weak sources of gamma rays and x-rays can be detected and measured. Combined with extraordinary sensitivity, counters are rugged, stable, simple to operate, and the results of measurements made with them lend themselves to easy interpretation.

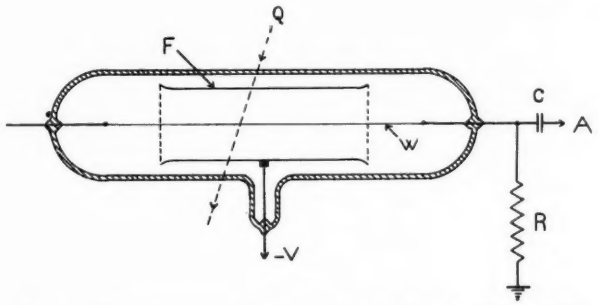

Fig. 1. Diagram showing fundamental principles of a Geiger-Müller counter.

Geiger-Müller tube counters are not particularly new instruments. They were invented in 1928 by Professor H. Geiger and W. Müller,[1] as an outgrowth and great improvement of the Geiger counter, or point counter, which had been in use for many years for counting alpha particles. Since their invention, tube counters have been adapted to a large variety of uses in physical laboratories. They have, indeed, become one of the physicist's most powerful tools for measuring weak radiations.

Three general types are now in use: (1) gamma-ray counters, suitable for measuring gamma rays, x-rays, and cosmic rays; (2) photo-electric quantum counters, which combine the characteristics of photo-cells and counters, and are used for measuring weak ultra-violet light, and (3) particle counters, for measurements of alpha, beta, and H particles. Of these forms, there are various mechanical modifications, made to meet the requirements of particular problems.[2] The present paper deals with counters of the first type, which we have used for locating radium and for making gamma-ray measurements during the last two years.

1. CONSTRUCTION AND PRINCIPLE OF OPERATION OF COUNTERS

A counter apparatus consists of: the counting tube (counter), an amplifier, usually employing radio tubes, a recording device for registering the number of discharges of the counter, and a suitable source of (negative) high voltage for the counting tube. The negative voltage is usually between 500 and 1,500 volts, depending on the kind of counter used.

The principle of operation of a Geiger-Müller counter (G-M counter) is explained

[1] H. Geiger and W. Müller, Phys. Zeits., 1928, **29,** 839; 1929, **30,** 489; 1929, **30,** 523.

[2] An extensive article describing the construction and use of Geiger-Müller counters is in preparation for the Review of Scientific Instruments, by one of us (G. L. L.). A preliminary report of some of the work has been given: G. L. Locher, Phys. Rev., 1935, **47A,** 326.

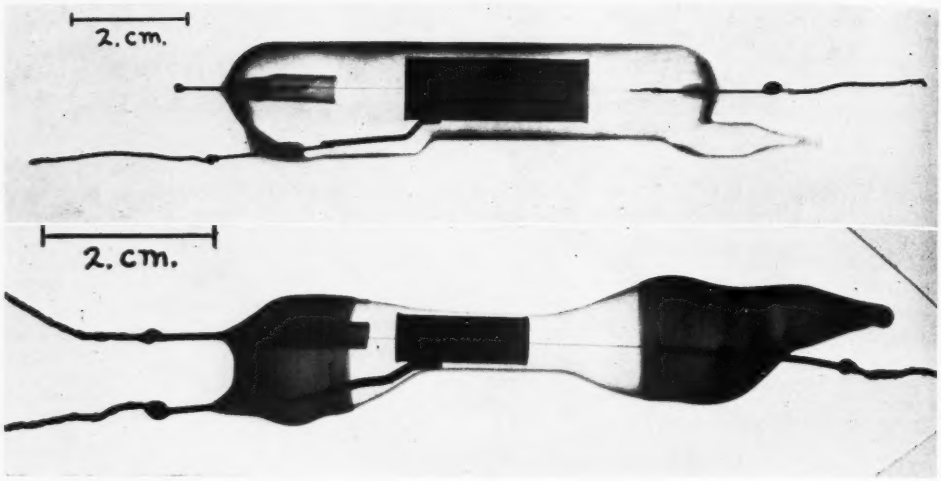

Fig. 2 (*above*). Gamma-ray type counter, suitable for gamma rays, x-rays, and corpuscular cosmic rays.
Fig. 3 (*below*). One type of x-ray counter, suitable for gamma-ray measurements in cases in which the intensity is relatively high.

by reference to Figure 1. A wire, W, is stretched along the axis of a hollow metal cylinder, F, enclosed in a glass tube. After suitable treatment of the electrode surfaces, the tube is filled with a suitable gas, usually at about 1/10 atmospheric pressure, and sealed off. A negative voltage, V, is applied to the cylinder-electrode (cathode); the wire (anode) is connected through a small condenser, C, to a vacuum-tube amplifier, A (or a string electrometer), and through a high resistance, R, to ground. The value of V is adjusted so that it is *nearly* enough to cause a brush discharge between the electrodes. When in this sensitive state, any ray, Q, passing through the tube and liberating one or more ions in F, initiates a small gas discharge between the electrodes. This discharge, recorded by A, is automatically quenched, within a few thousandths of a second, as a result of the lowering of the voltage across the counter by the Ri drop of potential in R (where i is the ion-current conducted through the counter). After this, the counter is again sensitive.

It is evident from the foregoing that the high sensitivity of the counter arises from the fact that it *counts the number of individual rays* passing through it, whereas other apparatus for measuring ionization require many rays to give detectable ionization. A G-M counter resembles an ionization chamber or electroscope, in that the radiation measured must produce ions within the sensitive region, by photo-electric action or otherwise, but it differs from an ionization chamber or electroscope, in that each ionizing particle liberated in the sensitive volume is automatically subjected to very large amplification *within the counter*. The output of this discharge is adequate for further amplification with a vacuum-tube amplifier. In this way, energy amplifications of many millions are very easily obtained.

II. EFFICIENCY AND SENSITIVITY TO GAMMA RAYS

The sensitivity of any particular counter to gamma rays is determined, especially, by its longitudinal cross-sectional area; other factors include the thickness of the glass tube and metal cylinder, and the kind and pressure of the gas contained in it. However, it is not to be inferred that the useful sensitivity increases with the size of the counter, without limit, even when the intensity of the gamma radiation to be measured is almost infinitesimally small. The

size of counter most suitable for a particular purpose must be determined from considerations of the intensities of radiation to be measured, the recovery-time of the counter and electric circuits, and the accuracy desired in the measurements. In general, the most suitable size for any purpose varies inversely with the intensity of radiation to be measured.

Figure 2 is an x-ray photograph of a counter of a type that we find to be very suitable for most gamma-ray measurements. Its cathode is 1.0 cm. in diameter and 3.0 cm. long. The gas is argon with a little oxygen, at a pressure of 8.0 cm. of mercury.[3]

The gamma-ray efficiency of a counter may be defined as the ratio of the number of its discharges, due to the gamma rays, within any interval, to the number of gamma rays passing through its sensitive region, in the same interval. The approximate efficiency can thus be determined by measuring the counting rate due to gamma rays from a known quantity of radium, at a measured distance from the counter. This procedure is illustrated by the following determination, made with a counter like that shown in Figure 2, using 0.01 mg. of radium in a thin-walled container at a distance of 150 cm. from the counter:

Spontaneous counting rate, due to cosmic rays and stray radio-activity of the building....8.42 per min.
Total counting rate with 0.01 mg. Ra at 150 cm.....19.65 per min.
Rate due to radium only is, thus,.....11.22 per min.
(133 per cent increase in rate, over background rate)
No. gamma rays per sec. from 0.01 mg. Ra[4].....640,000 (approx.).
Hence, the gamma-ray intensity at 150 cm. from the source is.....2.26 per sq. cm. per sec., or 135.6 per sq. cm. per min., approximately.
So the approximate efficiency of the counter for these gamma rays is: $11.22/(3 \times 135.6) = 0.028$, or *2.8 per cent.*

The efficiency of a counter of the same diameter, but five times as long (hence of five times as great longitudinal cross-sectional area), was determined similarly, for comparison. The spontaneous counting rate of the longer tube is five times that of the short one; the percentage increase in rate, due to radium gamma rays, and the gamma-ray efficiency, were found to be *very nearly the same as those of the short tube.*

The amount of "background," or spontaneous counting rate, of a counter sets a lower limit on the intensity of radiation that can be measured. If the size of the counter is increased, its response to the gamma radiation being measured, and its background rate, increase in very nearly the same proportion, so the "useful sensitivity" remains about the same.

The upper limit of the intensity of radiation that can be measured with any counter is determined by the recovery-times of the counter and amplifying circuits, particularly by the former. The shortest recovery-time so far attained in a G-M counter is about 0.0007 second. Even with such a short recovery-time, it would be impractical to make measurements with gamma radiation whose intensity exceeds 20,000 quanta per second, falling on a counter of 1.0 sq. cm. sensitive area. (This corresponds to about 40.0 mg. of radium at 1.0 meter.) Indeed, it is not usually practical to use radiation of greater intensity than that from about 3 or 4 mg. of radium at one meter, unless very elaborate amplifying and recording apparatus are used. For measurements of stronger radio-active sources, one can, of course, increase the source-to-counter distance, or diminish the sensitive area of the counter exposed to the radiation, by using a heavy shield with a small window.[5] Another very good method is to use a counter of very small size, like that shown in Figure 3. Such counters have two special advantages: their recovery-time is very short (facilitating rapid counting), and the background rate is usually negligibly small. The counter shown has a background rate of 2.0 per

[3] This tube was developed by one of us (G. L. L.), with the assistance of Mr. A. G. Nester, for cosmic-ray measurements in stratosphere balloon flights. In the last three stratosphere flights, 559 such counting tubes have been used.

[4] Rutherford, Chadwick, and Ellis, "Radiations from Radio-active Substances," p. 503; Cambridge University Press, 1930.

[5] Lead shot, in strong containers, make convenient demountable shields. About 1.7 cm. of shot is equivalent to 1.0 cm. of solid lead.

minute, and a gamma-ray efficiency of approximately 2.5 per cent for Ra gamma rays. It was designed for x-ray measurements, so the central portion of the glass tube is of very thin Pyrex, to minimize wall absorption.

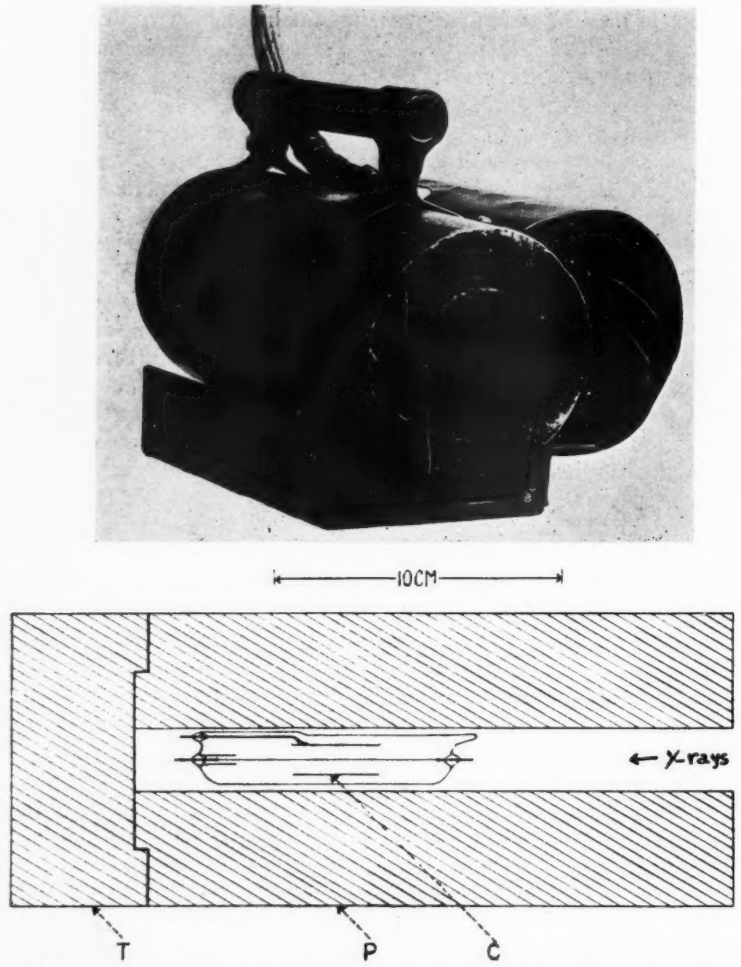

Fig. 4. Shielded counter for directional measurements: *a* (*above*), view of lead shield and vacuum-tube amplifier; *b* (*below*), cross-sectional view, showing position of counting tube.

A *directional counter* for gamma rays can be arranged by shielding the tube with a few centimeters of lead on all sides except that on which the radiation falls. An arrangement of this sort is shown in Figure 4. The shield reduced the background counting rate from about 8 per min. to 3.5 per min. The counting rates of this tube, due to 1.935 mg. of radium (in Pt needle), placed at various distances from the counter, are given in Table I. Since the intensity of radiation from a compact source varies inversely with the square of the distance from the source, the product of the intensity and the distance squared should be constant, if scattering and absorption of the rays are negligible. In the case of a G-M counter, the counting rate is a measure of the intensity, so the product of the counting rate and the square of the

distance should be constant for a given source.

TABLE I.—RESPONSE OF A SHIELDED COUNTER TO GAMMA RAYS FROM 1.935 MG. RADIUM. SPONTANEOUS COUNTING RATE: 3.47 PER MINUTE

D = counter-radium distance, in meters	R = counting rate due to radium: no. per min. R, measured	RD^2
2.0	217.7	870.8
3.0	93.5	841.5
4.0	56.1	897.6
6.0	24.2	871.2
8.0	12.0	769.9
	R, extrapolated.	Mean: 850.2
1.0	850.	(850)
0.1	85,000.	(850)

Calculated rates for other quantities of radium. at various distances, based on: $RD^2/Q = 850./1.935 = 440$ (approx.)

Q = quantity of radium, in milligrams	D = distance, in meters	R = computed counting rate
100.0	10.0	440.
100.0	1.0	44,000.
10.0	10.0	44.
10.0	1.0	4,400.
10.0	0.1	440,000.
1.0	10.0	4.4
1.0	1.0	440.
1.0	0.1	44,000.
0.0001	0.1	4.4

The constancy of RD^2 shows that the inverse square law is applicable to this apparatus, within the limits of accuracy imposed by variation of the efficiency of the counter, due to filtering of the rays, and small spurious effects arising from the scattering of the rays by air and surrounding objects. This is very convenient, since it makes possible the extrapolation of values of R corresponding to other values of D, once the product is known. The rates given in the lower part of Table I are extrapolated for other quantities of radium at various distances, on the basis of $RD^2 = 850.$, for this counter, kind, and amount of radiation.

Very minute quantities of gamma-ray emitting substances can be measured with a counter apparatus. A convenient measure of the minimum amount of gamma radiation that is "easily detectable," with any counter and configuration, is the intensity of radiation which increases the counting rate by an amount equal to the background rate. Thus for the shielded counter (Fig. 4), about 0.00002 mg. of radium, at 5 cm. distance, gives an increase equal to the background rate. The un-shielded counter (Fig. 2) has a considerably higher sensitivity than the shielded one, because the area exposed is larger, and because the gamma radiation is incident through the side, instead of the end of tube. Only 0.000008 mg. of radium, at 5 cm. distance, is required to double the background counting rate. This is roughly equivalent to the *natural radium content of* $^1/_{12}$ *cu. ft. of ordinary earth!* So it is evident that a counter apparatus is highly suitable for detecting small amounts of radio-active contamination.

Response of the counter shown in Figure 2 to some other weak radio-active sources is as follows: to 1.0 g. uranium, sealed in a glass tube, 10.0 cm. from the counter, 163.5 per cent increase in rate; to 1.0 g. thorium, arranged similarly to the uranium, 54.5 per cent increase in rate; to 100.0 g. potassium chloride, sealed in a glass tube and placed against the counter, 8.4 per cent increase in rate (100.0 g. KCl corresponds to about one-millionth mg. of Ra, in gamma-ray activity).

III. ILLUSTRATIONS OF THE USE OF COUNTERS FOR GAMMA RAYS

It is interesting to note that the shielded counter (Fig. 4) was built about two years ago, to meet an emergency. This arose when a 2.0-mg. ampoule of Ms Th_1 solution was broken, by freezing, in a large lead block that served as a container. With the aid of the counter apparatus, more than 90 per cent of the material was recovered. All vessels, gloves, extracted solutions, and residues were tested for gamma-ray activity at frequent intervals during the extraction processes. The advantages of using a G-M counter for detecting radio-active contamination and for measuring small amounts of gamma radiation became evident at that time.

The second application of this apparatus was for measuring the gamma-ray penetra-

Fig. 5. Convenient portable counter apparatus, employing vacuum-tube amplifier and 10-to-1 voltage multiplier, in use.

tion and scattering from a 4.0-gram radium bomb. The intensities of radiation at various points in adjoining rooms were measured, and expressed in terms of milligrams equivalent at a distance of 1 meter. The highest value measured (bomb open), amounted to 3.5 mg. at 1.0 meter. The approximate absorption coefficient of the radiation at that point was measured, by successfully taking the counting rates with and without a $^3/_{16}$ inch lead shield before the counter. The coefficient so determined was 0.735 per cm. of lead, as compared with the known value of 0.78 for a mixture of RaB and RaC rays.[6]

The chief advantages of a counter apparatus over electroscopes, for *locating* lost radio-active material, lie in the great speed of detection and in the high inherent sensitivity of counters. We have used counter apparatus for locating lost radium needles on four occasions. The radium contents of these needles were, respectively, 1.0 mg., 40.0 mg., 10.0 mg., and 1.0 mg. Two were found in sewer traps of hospitals, one was in an ash heap, and one was on a hospital floor. In each case, the location was made in a few minutes, without the necessity of measuring counting rates, since the gamma radiation was immediately detected when the counter was brought into the vicinity of the radium. In one of these cases, a continuous but unsuccessful search for the tube (1.0 mg.) had previously been carried on for some hours, with electroscopes.

In the event that the radio-active material sought is obscured by a large amount of massive material, the procedure would be, of course, to make gamma-ray measurements at numerous points in the vicinity. From these, the approximate position of

[6] A counter apparatus is also excellent for detecting x-ray leakage. The efficiency of the counter is, of course, dependent on the wave length. For x-ray measurements, a shielded counter is very desirable, because of scattering from surrounding objects.

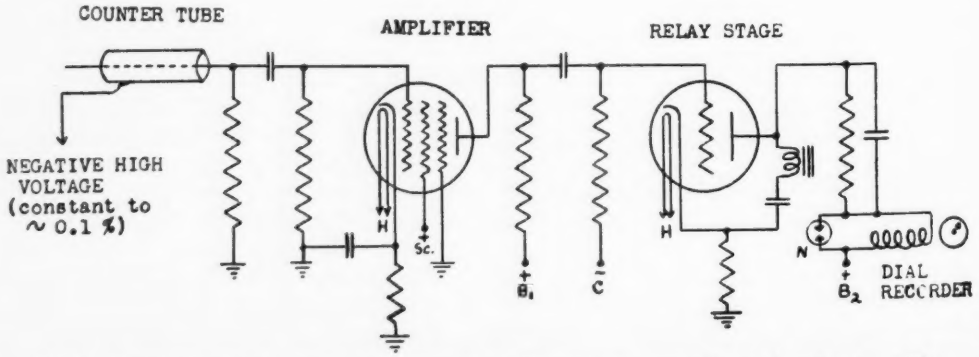

Fig. 6. Electric circuit used for precise measurements of gamma-ray sources of low and medium intensities.

the material sought could be calculated by simple triangulation and the assumption of a value of the absorption coefficient of the intervening material for the gamma rays emitted. We have never yet found this procedure necessary.

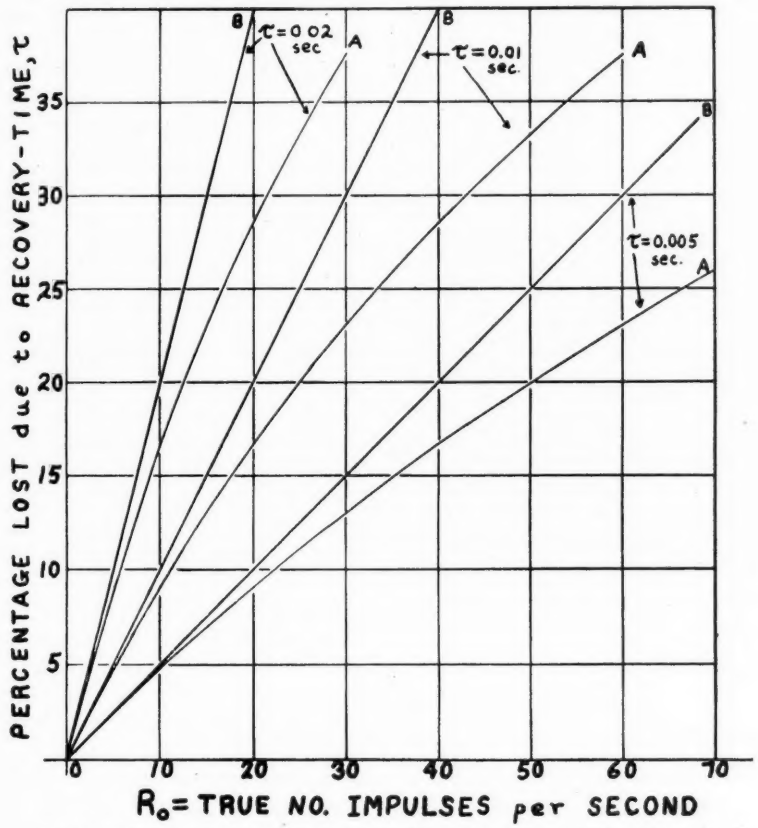

Fig. 7. Typical correction curves for resolving-time losses, based on formulæ of Danforth.

IV. TYPE OF COUNTER APPARATUS

The type of counter set to be used for any purpose depends on several factors, namely: the accuracy required in measurements, the availability of alternating current for the power supply, the permissible size and weight of the apparatus, and the cost of construction. For locating radio-active material, a portable apparatus of light weight, operating entirely from dry batteries, is most suitable. For precise measurements, it is desirable to use more elaborate equipment, including a source of very constant high potential for the counting tube and a rapid recorder for the counter impulses. Such equipment is most conveniently operated from an A.C. lighting circuit.

Figure 5 shows a very light dry-battery-operated portable set in use. The counting tube and vacuum-tube amplifier are contained in a small tubular unit that is attached to the power supply by a flexible cable. The power supply for the amplifier (3 volts and 45 volts) and the high voltage supply (900 volts) come from small dry batteries contained in the carrying case shown. The 900-volt supply is obtained from a 90-volt dry battery, by means of a ten-to-one D.C. "voltage multiplier." The use of this multiplier greatly reduces the

weight of the equipment and makes the cost of the batteries small. The counter discharges are heard as sharp clicks in a telephone head-set worn by the operator.

Figure 6 shows the type of amplifying and recording circuit that we usually employ for precise gamma-ray measurements. This circuit employs a high-gain amplifier and gas-tetrode relay circuit. It is very satisfactory for use with a G-M counter of any type, in instances in which the counting rate does not exceed 1,000 impulses per minute. The number of impulses is registered on a dial recorder. A neon or argon glow lamp, N, is also provided for visual observation (from a distant point, for example), or for the photographic registration of the individual impulses. For accurate measurements, the negative potential applied to the counter cathode must be held very constant. We accordingly use a Street-Johnson regulated high-voltage source,[7] whose output is constant to better than 1 part in 1,000, for any fluctuations in the A.C. potential. The entire apparatus is A.C. operated.[8]

V. CORRECTION OF COUNTER MEASUREMENTS

The types of error inherent in counter measurements are well known, and corrections for them can be applied with accuracy that is much better than the corrections of usual ionization measurements, unless the counting rates are very high. The chief errors of counter measurements are: (1) statistical error, arising from the finite number of impulses recorded, and (2), impulses not recorded because of the "resolving time" of the counting tube or recording apparatus. The "resolving time" of the apparatus is the time that must elapse between two successive impulses in order that both will be recorded. (It is approx. 0.015 sec. for the recording circuit shown in Figure 6.)

(1) The statistical error is $\pm 1/\sqrt{N}$, where N is the total number of impulses that occur during the observation; or the percentage error is $100/\sqrt{N}$. Hence the error is 5 per cent for 400 impulses, 3 per cent for 1,000 impulses, 2 per cent for 2,500 impulses, 1 per cent for 10,000 impulses, etc. All measurements given in this paper have statistical error of approximately 1 per cent.

(2) Correction for the number of impulses that are not recorded, due to the finite resolving time of the apparatus, must be added to the recorded number. The amount of this error is determined by the counting rate and the longest resolving time (τ sec.) of the apparatus. If $1/\tau$ is very large compared with R_0, the number of impulses per second, the error is negligible. As R_0 approaches $1/\tau$, the error increases rapidly, and accurate correction for it becomes more difficult. The reason for this is as follows: with good apparatus and slow counting rates ($R_0\ \tau = 0.001$ to 0.05), τ has a constant value; but at high counting speeds, τ varies with R_0 in a manner which depends on the particular apparatus. Two simple formulæ, derived by Dr. Danforth,[9] give, respectively, the approximate lower and upper *limiting* values for the correction. Both assume that τ has a definite value, and that the impulses arrive at random times. Formula A assumes that if one or more impulses arrive within time τ after a previous one, the latter are not recorded, but that the apparatus is made insensitive by the group only for time τ. Formula B assumes that each impulse makes the apparatus insensitive for time τ, immediately after its arrival, independently of any other impulses. Neither assumption is wholly correct, especially for high counting speeds, but they

[7] J. C. Street and T. H. Johnson, Jour. Frank. Inst. 1932, **214**, 155. The "first type" of voltage control is used. The tube for regulating the voltage is of type 57, which gives better regulation than a 24-A tube. G. L. Locher, Phys. Rev., 1934, **46**, 1047.

[8] A semi-portable counter set for gamma rays was demonstrated by one of us (J. L. W.) before the American Roentgen Ray Society, at the Atlantic City meeting of the Society, September, 1935, during the discussion of a paper by Dr. Robert B. Taft. This set is light in weight, but uses A.C. power, hence is not completely portable.

[9] W. E. Danforth, Bartol Research Foundation of the Franklin Institute unpublished communication.

are convenient for correction, under ordinary conditions. They are:

$$\text{(A)}\ R = R_0/(1 + R_0\,\tau), \text{ and}$$
$$\text{(B)}\ R = R_0\,(1 - R_0\,\tau),$$

where R is the measured counting rate per second; R_0 is the true counting rate per second, and τ is the resolving time. Curves representing these relations, for $\tau = 0.005$ sec., 0.01 sec., and 0.02 sec., are shown in Figure 7. The value of τ can be experimentally determined by applying evenly spaced impulses to the apparatus, through the high potential supply, at increasing speeds, until the apparatus begins to fail to record them.

Illustration of approximate correction of all errors, in an hypothetical case: Background rate of counter, 4.0 per min.; resolving time of apparatus, 0.010 sec.; time of observation, 12 min.; number of impulses recorded, 3,600. Then the recorded rate, R, is: $3{,}600/12 = 300$ per min., or 5 per sec. The statistical error $= \pm 100/\sqrt{3{,}600} = 1.67$ per cent, or $\pm$ 5.0 per min. Error due to τ is between: (A) 4.78 per cent and (B) 5.0 per cent, with a mean value of 4.9 per cent, or 14.6 per min. Background rate: 4.0 per min. Hence the corrected rate is: $R_0 = 300.0 - 4.0 + 14.6 \pm 5.0 = 310.6 \pm 5.0$ per min., due to the radiation. The corrections applied are thus, 10.6/310.6, or 3.4 per cent of the true rate, in this case.

We are indebted to Herbach and Rademan, Inc., of Philadelphia, for the construction of part of the amplifying and recording equipment used in these experiments, and for the loan of the set shown in Figure 5.

MANAGEMENT OF CERVICAL METASTATIC EPIDERMOID CARCINOMA[1]

By WRIGHT CLARKSON, M.D., *and* ALLEN BARKER, M.D., *Petersburg, Va.*

CANCERS about the mouth, pharynx, and larynx rank among the deadliest of neoplasms. This high mortality is not the result of direct extensions of the original lesions, but of lymph node metastases. Many of the primary lesions originating about the head and neck, particularly those beginning in the mucous membranes, are being treated improperly. Lymph drainage areas are often altogether ignored until inoperable metastases have occurred, or inadequate irradiation is given so as to render the growths radioresistant and therefore incurable.

Timidity in the treatment of a malignant neoplasm, whether it be by radiation or by surgery, is almost inexcusable. One must have the courage to be scientifically radical when treating cancer.

The successful management of epidermoid carcinomas of the cervical lymph nodes demands a broad knowledge of the proper application of external and interstitial irradiation, of surgery, of a combination of these methods of treatment, and an adequate knowledge of tumor pathology.

The primary lesion should always be subjected to a thorough microscopic examination, and the method of treatment or combination of methods to be used in each case must be determined by a careful correlation of the microscopic pathology with the history and physical examination.

The dissemination of malignant cells is a danger against which the physician must carefully guard. Since forceful manipulation of a tumor is apt to facilitate this dissemination, care must be taken not to traumatize the lesion during examination. As a precautionary measure against the spread of malignancy, adequate preoperative irradiation should always precede the biopsy by about one week.

In removing tissue for examination, it is important to remember that the microscopic appearance may vary widely in various parts of the same neoplasm. Therefore, sections should be taken from various parts of a tumor. Whenever surgically practicable, one should completely remove an original growth that involves one of the upper mucous membranes, taking a wide margin of healthy tissue. This gives ample opportunity for a thorough microscopic study of the neoplasm and is the best method of safeguarding against a local recurrence. The complete removal of an epithelioma of the skin, however, is often undesirable for cosmetic reasons; usually it is not necessary, because the gross appearance and a properly made biopsy will give sufficient information, and the tumor's being more accessible makes it easier completely to destroy the growth by means of irradiation.

Our cases are classified grossly as follows: (1) those having no palpable nodes; (2) those with palpable nodes that are considered operable; (3) those with palpable nodes that are inoperable. Each group requires its own type of therapy, with variations dependent on the individual case and the histologic findings.

Each group is sub-divided into four grades according to Broders' histologic classification, *i.e.*, Grade I, Grade II, Grade III, and Grade IV. The experience of some observers in the past appears to have indicated that it is not always possible to determine the radiosensitiveness of a tumor by its histologic grading, but the radiosensitiveness of a neoplasm can be so determined accurately, provided one takes into consideration the radiosensitiveness of the tissue or origin and compares the tumor

[1] Read before the Radiological Society of North America, at the Twenty-first Annual Meeting, in Detroit, Dec. 2–6, 1935.

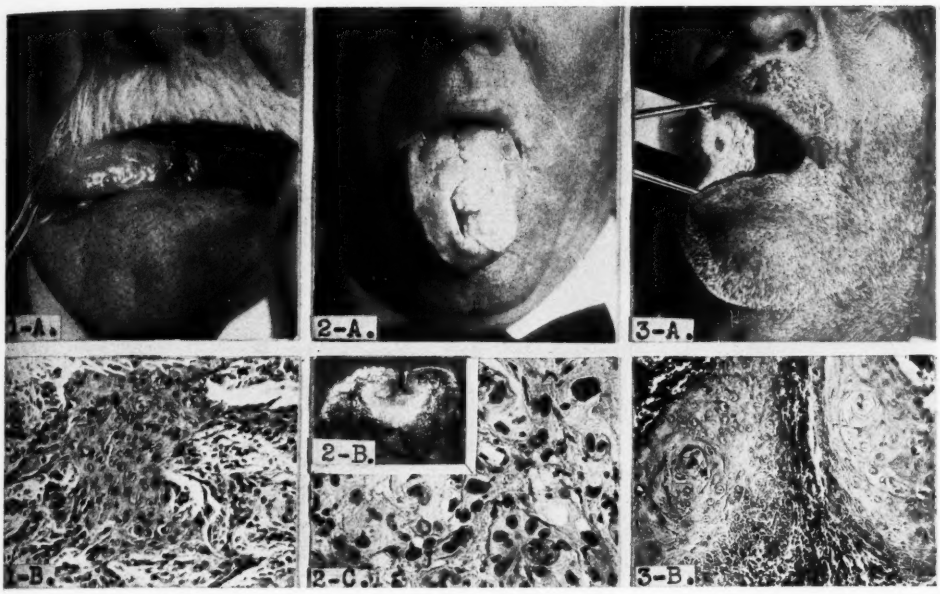

Fig. 1-*A*. Grade III cancer of the tongue, with growth extending to the midline, and small nodes in neck. Roentgen therapy was instituted; removal of primary growth; radon implantation. There was no return of the cancer at the last examination, two years later. Note malignant but fairly radiosensitive cancer tissue shown in photomicrograph (Fig. 1-*B*).

Fig. 2-*A*. Grade IV cancer beginning in leukoplakia which had existed ten years; metastases to neck and liver. Note cancer developing about the fissure shown in cross-section of tongue after removal (Fig. 2-*B*). Microscopic sections show highly radiosensitive type of tissue (Fig. 2-*C*).

Fig. 3-*A*. Typical Grade I cancer developing in area of leukoplakia, buccal surface. Figure 3-*B* shows highly radioresistant type of cancer tissue but one that rarely metastasizes; this type may be cured if properly removed. The leukoplakia must be carefully eradicated or cancer may develop again.

only with tumors of the same histologic classification. For instance, with the exception of the melanomas, which, strictly speaking, should not be placed in this classification, the radiosensitiveness of epidermoid carcinomas increases in direct proportion to the amount of anaplasia, and we believe this rule will hold true of all neoplasms when considered separately within their own histologic classification.

GROUP I

In considering the first major group into which our cases are divided, we find some controversy; that is, radiologists as a rule advocate external irradiation, while many surgeons advise complete block dissection of the neck. There is, however, evidence that lymph nodes act as a barrier to the spread of cancer and, therefore, it is wise to preserve them when possible. Prophylaxis by proper external irradiation is as successful as surgical prophylaxis. Widmann (1) reports a group of patients in whom only 17 per cent of those receiving proper external therapy developed cervical metastases, while 51 per cent of the non-irradiated cases developed uncontrollable metastases. These statistics compare favorably with those of the most experienced surgeons.

The patients in this group should be given the benefit of thorough external irradiation. Each side of the neck, including the base of the brain and the clavicles, should receive a total of from 2,000 to 3,500 roentgens, the exact amount depending upon the size of the primary growth, its duration, the amount of invasion of the surrounding tissues, the radiosensitiveness of the lesion, the patient's physical condition, and the reaction of the individual to the irradiation. The treatment should be

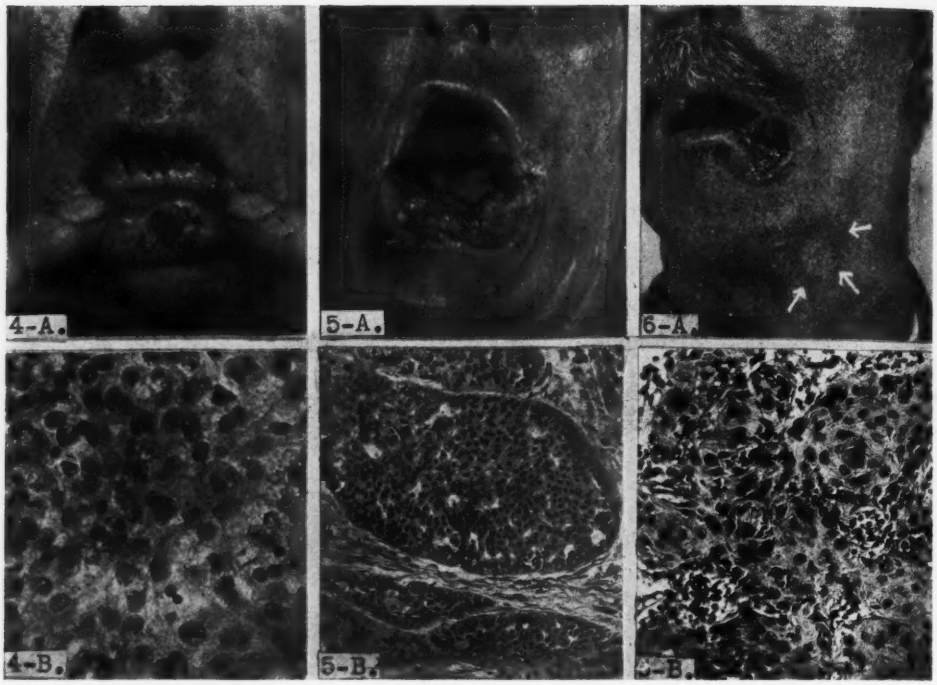

Fig. 4-*A*. A rather harmless looking little lesion with no nodes, but photomicrograph (Fig. 4-*B*) shows Grade IV carcinoma. These lesions cannot be recognized without microscopic examination. They are fatal unless diagnosis is made and growth and lymph drainage areas are intensely irradiated at early stage. This patient refused irradiation and died soon after extensive operation by an eminent surgeon.

Fig. 5-*A*. Horrible looking cancer of the lower lip, Grade III, with metastatic nodes. Note photomicrograph, Figure 5-*B*. Patient well to-day, 8 years after photograph was taken. Treatment: extensive external irradiation and removal of primary lesion with endotherm.

Fig. 6-*A*. Cancer of lip, Grade II, see Figure 6-*B*. The mass below the jaw, which was firmly fixed to the bone, was not sensitive and was slowly but progressively enlarging. Massive doses of roentgen ray were given; no other treatment. Well to-day, 9 years later.

given in daily doses over a period of about four weeks. If metastases do not appear later, no further treatment is necessary. However, if after proper irradiation metastatic nodes do appear, they should be removed surgically, if possible, for further irradiation will not control them.

GROUP II

The successful management of the second group is dependent upon a thorough knowledge of tumor pathology, upon the radiologist's ability to administer scientific external and interstitial irradiation, and upon the criteria for operability.

Operability is often quite difficult to determine, but as the experience of the radiologist increases, more definite and accurate criteria are established, with the result that fewer cases are placed in the surgical group. Quick's (2) criteria for operability are as follows: "Surgical dissection of the neck, when done, is unilateral, but the most radical possible. Dissection is limited to fully differentiated epidermoid carcinoma, palpable involvement unilateral, capsule of the node or nodes presumably intact in patients presenting good physical condition, and in whom the primary growth is either controlled, or gives promise of complete controllability."

Average statistics of radical neck dissections show a high mortality from recurrences, and our records show a survival of few cases so treated. The procedure is, therefore, limited to a few carefully selected

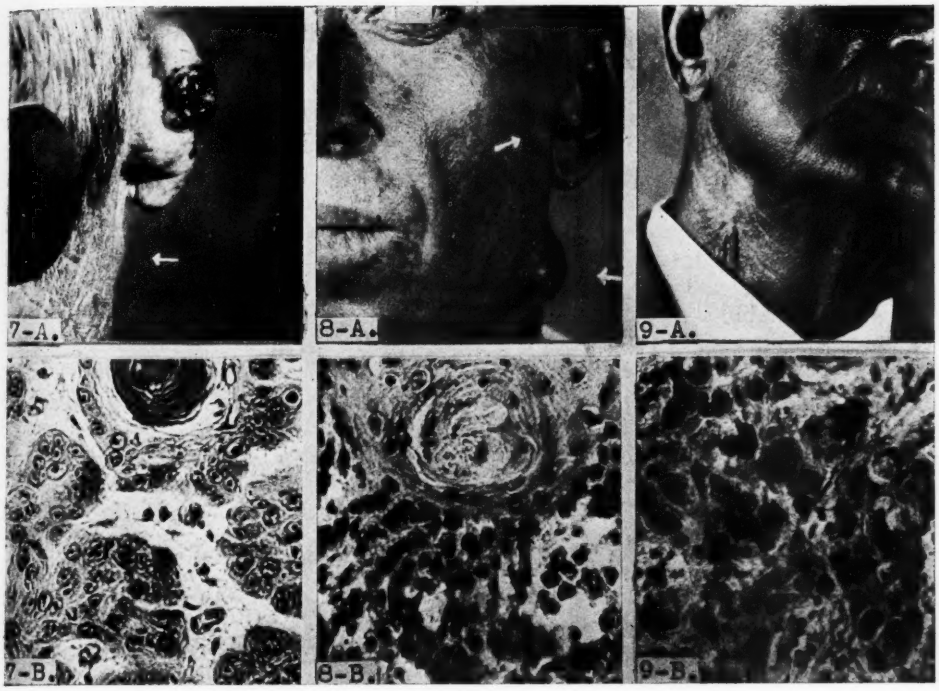

Fig. 7-*A*. Cancer of pinna, cervical metastases, treated by roentgen therapy and implantation of nodes. See photomicrograph, Figure 7-*B*, Grade II. Patient well 3 years.

Fig. 8-*A*. Metastatic cancer following electric coagulation of skin lesion in a physician's office. Photomicrograph (Fig. 8-*B*) taken from node, Grade III. Intensive external irradiation was given; only the isolated mass shown in photograph was removed. Patient well 5 years.

Fig. 9-*A*. Photograph showing skin in good condition; patient clinically well three and one-half years after 3,000 r had been given to each side of the neck and 9,000 mc.-hr. interstitial irradiation for cancer of pharynx, Grade IV. Note extremely anaplastic cells removed from metastatic lymph nodes; photomicrograph, Figure 9-*B*.

cases. The method of choice is intensive external irradiation as advocated in the first group of cases, followed, as soon as the skin reaction subsides, by surgical removal of isolated palpable nodes and interstitial irradiation of any palpable masses of nodes that may remain. Electrosurgery is preferred for the removal of the nodes (Fig. 8).

At this time it is important to emphasize the fact that proper interstitial irradiation usually requires surgical exposure, as it is often impossible accurately to implant, through the skin, a node or nodes with radium element or radium emanation.

Grade I neoplasms (Fig. 3) are slow to metastasize, but once metastases have occurred no combination of irradiation is likely to produce a cure. In this type of malignancy, with multiple intact nodes, radical surgery following thorough external irradiation offers the best hope of eradicating the growth. If only a single palpable node is present, it is often wise to remove only this node. In either case, all areas from which nodes are removed should be implanted with radium emanation, the dose of irradiation being limited only by normal tissue tolerance.

The Grade II metastases are also relatively radioresistant, and they may be treated in somewhat the same manner as the Grade I tumors, although these metastases, if small, may yield completely to proper external and interstitial irradiation (Figs. 6 and 7). Large nodes remaining after intensive external irradiation should

be removed by means of an endotherm; radical neck dissections are seldom indicated in neoplasms of this grade.

The relatively anaplastic Grade III metastases should be treated with a combination of external and interstitial irradiation. In most of these cases surgical removal of metastases is neither wise nor necessary. After the skin reaction from thorough external irradiation has subsided, any remaining palpable nodes should be implanted with radium emanation (Figs. 1 and 5).

The radiosensitive Grade IV metastases may often be trusted to thorough external irradiation alone, but even in these cases implantation therapy is a wise precaution and should always supplement external irradiation when the metastatic nodes are large (Fig. 9).

Recurrences often occur even though proper external and interstitial irradiation has been given, and these nodes, if still operable, should be subjected to radical dissection because additional irradiation is practically useless.

GROUP III

Inoperable cervical nodes, irrespective of their grade, usually present a problem for irradiation only; however, an inoperable case may occasionally be made operable by proper irradiation. External and interstitial irradiation should be given in massive doses. Many of these patients can be made comfortable for a few months or years and occasionally a cure may result when the metastases are highly radiosensitive.

One of the most perplexing problems confronting radiologists at this time is, what disposition should be made of the many inoperable cases in which the tumors have previously been rendered radioresistant by improper and inadequate irradiation? It may seem wrong to refuse to further irradiate some of these cases. Certainly, each one of them should be carefully analyzed and treated if there remains the slightest hope of a cure or substantial improvement, but most of them cannot be materially benefited by further irradiation and there is considerable doubt in our minds as to the advisability of attempting further local treatment in these cases.

During the past few years we have irradiated the gonads and pituitary glands of these hopeless patients. This appears to retard the growth to some extent, but our experience so far has not been sufficient to justify definite conclusions.

MELANOMAS

The metastases resulting from melanomas comprise a radioresistant group of tumors in which, immediately following proper pre-operative irradiation, a radical operation should always be performed, provided all of the known metastases can be removed with a reasonable degree of safety.

LETHAL DOSE AND TISSUE TOLERANCE

Scientific irradiation therapy requires an accurate knowledge of the lethal dose of different types of irradiation for various types of neoplasms, as well as a knowledge of the tolerance of normal tissues to the same irradiation. The fractional dose technic has opened new avenues of approach to neoplastic diseases with roentgen irradiation. By this method it is possible to deliver from three to five skin erythema doses to the deep cervical glands and still permit a rapid recovery of the normal tissue. The time factor is extremely important; the total dose should be divided into equal daily doses administered over a period of four weeks. Coutard's method (3) of applying high voltage roentgen irradiation with low intensity apparently gives better results than the more recent high intensity technics.

Irrespective of the technic of external irradiation used, it is impossible to deliver to deep cervical glands the seven to ten skin erythema doses which Martin, Quimby, and Pack (4) have shown to be necessary for the complete destruction of an adult carcinoma. Therefore, it is imperative to supplement external irradiation with interstitial therapy, since a large percentage of metastases originate from a low

grade squamous-cell carcinoma. Reference to standard tables of dosage measurements indicates that it requires 10,000 millicurie-hours to deliver 10 skin erythema doses to a tumor mass 5 cm. in diameter, and 6 skin erythema doses to a mass 7 cm. in diameter. Such a dose will require approximately 80 millicuries of radium emanation to be left in the tissues until completely destroyed. With the aid of such figures, the amount of emanation necessary to sterilize a metastatic mass may be determined accurately. The emanation should be divided into implants of not more than 3 mc. each, and they must be spaced carefully so as to distribute the irradiation evenly. Although roentgen irradiation will materially reduce the necessary dose of interstitial irradiation, it is always wise to apply dosage up to the limits of tissue tolerance.

COMPLICATIONS AND SUPPORTIVE TREATMENT

Among the more serious complications arising in the treatment of malignancy is the presence of infection. In these cases interstitial irradiation is contra-indicated until the infection has subsided, and since the strings attached to removable implants assist drainage, they are usually preferable to permanent radon seeds.

Small daily doses of external irradiation are more beneficial than massive doses in treating infections, and, therefore, it is well not to exceed a daily dose of 100 r for about ten days. Accumulations of pus should always be evacuated by means of an endotherm as soon as they become localized and fluctuant.

By making a careful analysis of the general physical condition, and by keeping a close watch for such co-existing diseases as syphilis, diabetes, and cardiorenal or vascular disease, one may frequently save a cancer patient who would otherwise succumb. Likewise, much may be accomplished by giving general supportive treatment to these patients when they show signs of inanition. For instance, most patients with advanced cancer have a deficiency of hydrochloric acid in the stomach, and correcting this by intravenous injections or by giving the acid by mouth often proves beneficial.

The administration of vitamin concentrates will improve the general condition of the patient, and they should be given whenever specifically indicated; but it is possible for these concentrates to stimulate cancer growth also, and, therefore, their proper place in cancer therapy must await further experimentation. The same thing may be said about the administration of insulin. Its proper administration in cases complicated by diabetes is usually imperative in order to preserve the integrity of the skin that is being irradiated, and in non-diabetics it will increase appetite and thus prove temporarily beneficial to the patient, but no one can be certain at the present state of our knowledge about cancer that malignant metastases are not likewise stimulated. Therefore, for the present it may be well to confine its use to diabetics and to non-diabetics in a state of extreme inanition. In the latter case everything possible should be done to support the patient rather than direct all of our attention to the cure of the neoplasm.

SUMMARY

(1) The present high mortality rate from carcinomas of the upper mucous membranes is largely the result of a lack of proper treatment of the areas of lymph drainage by many physicians who attempt to treat the primary lesions.

(2) Pre-operative irradiation should always precede biopsy and all other forceful manipulations of the primary lesion.

(3) The possession of a thorough knowledge of the various methods of treatment, of adequate knowledge of tumor pathology, and of sufficient courage to be scientifically radical are absolutely essential when treating cancer. Careful attention must be paid to the lethal dose of irradiation for the various types of neoplasms, and whenever indicated the irradiation must be carried to the limits of tissue tolerance.

(4) The radiosensitiveness of an epidermoid carcinoma increases in direct propor-

tion to the amount of anaplasia, and this rule probably holds true of all neoplasms when considered separately within their own histologic classification. Therefore, sections should be taken from various parts of the primary growth to insure accurate grading and the direction of treatment accordingly.

(5) Prophylaxis is left to external irradiation alone. All cases with metastatic nodes are treated principally by a combination of external and interstitial irradiation. The operable nodes that may then remain are removed by means of an endotherm. Radical surgery is resorted to only in operable cases of melanomas and Grade I carcinomas with extensive metastases.

(6) In cases of infection, small daily doses (100 r) of external irradiation should be given first for about ten days; pus collections should be evacuated with an endotherm and in cases in which implantation therapy is used, removable seeds are advised because the strings facilitate drainage.

(7) Insulin and vitamin concentrates will improve the appetite and general condition of cancer patients, but no one can be certain at the present state of our knowledge that malignant cells are not likewise stimulated. Therefore, for the present it may be well to confine their use to diabetics and to non-diabetics in a state of extreme inanition.

In closing, we wish to express our appreciation to Dr. A. C. Broders for his assistance in grading the neoplasms we are reporting here as illustrations, and to Dr. J. S. Horsley, Jr., for his assistance in removing the nodes shown in Figure 8.

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THE TREATMENT OF BENIGN UTERINE HEMORRHAGE BY IRRADIATION[1]

By JAMES J. QUINEY, M.D., *Easton, Pa.*

IT is not my intention to advance any new theories as to cause or methods of treatment but to review facts which are already well known.

It has been stated by Anspach in the first edition of his work that, "almost every form of benign uterine hemorrhage is favorably influenced by radium treatment." So far as my own personal experience is concerned, I have found the use of external irradiation by means of the roentgen ray extremely satisfactory and I now rarely use radium, thereby avoiding the surgical procedure necessary for its intra-uterine application.

The causes of benign uterine hemorrhage may be classified as follows:

1. Myopathic uterine changes;
2. Glandular hyperplasia of the endometrium;
3. Functional disturbances of the ovary or ductless glands;
4. General diseases of the heart, kidney, liver, circulatory organs, etc.

The hemorrhages may threaten life by producing anemia or they may be merely a constant source of annoyance.

Irradiation is undoubtedly the treatment of choice in cases of menorrhagia of the menopause associated with fibromyoma. It yields extremely satisfactory results in cases in which the fibromyoma does not exceed in size a four-months pregnancy and in cases of a fibrous uterus in which the possibility of malignancy has been eliminated by the history or by a curettage (1).

In cases of hemorrhage at or near the menopause it is considered proper by many radiotherapists to irradiate as for malignancy. Every attempt should be made, however, to eliminate malignancy by a bimanual and visual examination of the cervix, as advocated by Dr. J. Mason Hundley, of Baltimore, making use of Schiller's iodine test and by making a microscopic examination of the scrapings obtained by a careful curettage. I am more and more impressed with the necessity of this procedure. By observing these rules in all cases, disappointment to the patient and embarrassment to the therapist can be avoided.

In treating uterine fibromyoma it is immaterial as to whether the tumor is submucous, interstitial, or subserous (2). A pedunculated fibromyoma is not considered suitable for treatment. A degenerating or strangulated fibromyoma should be removed by surgical procedure unless there are very definite contraindications to an operative procedure. Fibromyomas of such dimensions that they extend above the umbilicus, or those causing pressure effects should also be removed surgically.

Pelvic infections are a definite contraindication to the use of radium but this statement does not so strictly apply to the use of the roentgen ray.

Neill, of Baltimore, is responsible for the statement that 75 per cent of all uterine fibroids are amenable to irradiation therapy, probably meaning radium. This number is increased when the roentgen ray is the therapeutic agent used. Neill also states in the same article that the response to irradiation in cases of uterine fibroid is very rapid, in some instances showing a great reduction within a few weeks; in other instances, disappearance occurs six months to a year after the bleeding stops and 80 per cent of the smaller and 50 per cent of the larger tumors disappear completely.

On Sept. 27, 1919, Dr. A. Beclérè, of Paris, presented a contribution to the Association of French-speaking Gynecolo-

[1] Read before the Pennsylvania Radiological Society, June 5, 1936.

gists and Obstetricians at Brussels. In this report he presented the statistics of 400 cases of uterine fibromyoma treated by x-ray in his own private practice from 1908.

The greatest number of cases occurred between 45 and 49 years of age; the fewest between 55 and 56 years of age.

Of the 400 cases, 15.5 per cent were intrapelvic and 84.5 per cent consisted of fibromyomas with abdominal projections—above the symphysis from 1 to 4 centimeters in 38 patients, and from 25 to 30 centimeters in 9 patients.

In the great majority of the patients the predominating symptoms consisted of metrorrhagia, more or less copious, prolonged and regular in appearance.

Treatments consisted of weekly applications of moderate dosage in preference to a monthly intensive dosage. Each weekly treatment consisted of two successive exposures, one to the right and one to the left of the median line of the abdomen just above the horizontal ramus of the pubes. Occasionally, because of retrodisplacements or when the fibromyoma occupied the concavity of the sacrum, a third exposure was directed toward the sacral region. If the dimensions of the tumor required it, six ports were used. Each exposure was localized on a circular surface, 10 centimeters in diameter, by means of a cylinder of lead glass. Beneath this cylinder of lead glass was placed a block of wood and, by means of compression, the surface was flattened and the distance between skin and ovary lessened. The distance used was from 7.2 to 8.8 inches and one milliampere of current was allowed to pass for from 10 to 15 minutes.

In 60 per cent of the 400 patients the course of treatment extended over a period of from two and one-half to three months. Twelve to 14 weekly treatments were given. In only four cases did radiotherapy fail, and, so Beclérè states in his article, with the more modern technic used at the time of writing his paper, even these four cases would have been cured. The metrorrhagia ceased and there resulted a suppression of the menstrual function.

The onset of hot flashes incident to the menopause was the signal for cessation of the treatment. The menses would occasionally reappear after several months, whereupon a small number of abdominal exposures became necessary. The size of the tumor was reduced from one to two centimeters in 12 patients and 16 centimeters in one patient. A corresponding reduction also took place in the transverse diameter of the uterus.

Since 1919, at the time these facts were presented, great improvements in equipment have been made, such as the enormous increase in the output of transformers, the construction of x-ray tubes in such a manner that the output of roentgen rays can be more readily regulated, the acquirement of a better knowledge of filtration, and the establishment of the r unit. These improvements have added materially in the administration of adequate dosage.

To-day there are several methods of treating these cases efficiently with the roentgen ray. A great change has occurred since 1919, when Beclérè presented his remarkable article.

Henry Schmitz (3), in a recent article, states: "The roentgen dose for the production of permanent amenorrhea is about 400 r with back-scattering measured in the mid-pelvis and attained through two fields, one suprapubic and one sacral. The kilovoltage should be 200 and the filter 0.5 to 0.75 mm. Cu plus 1.0 mm. Al." He warns of the necessity of standardization of the output of transformer and tube with r unit meters to attain the expected result.

With the above factors but little time is required to administer the 400 r unit (50 per cent) dose in the mid-pelvis; it is well, however, to divide the dose and give it over a period of time, making up the total loss in r units.

Schmitz also states: "The good end-results of irradiation treatment in the functional uterine hemorrhages was 316 in a total of 322, or 98.14 per cent, and the mortality was 0.66 per cent. . . . The

good end-results in bleeding uterine myomas was 103 in a total of 109 cases, or 94.5 per cent, and the mortality was 1.0 per cent."

For some time it has been our custom to treat through four 15 × 15 cm. areas, two anteriorly and two posteriorly, directing the central beam to the uterus and ovaries. The method employed is that advocated by Weatherwax using 200 kv., 5 ma., 0.5 mm. Cu plus 1.0 mm. Al, and using 650 r in the center of the pelvis.

At each sitting, 200 r is given over each area, making up the loss of each interval, until the desired number of r units have been delivered to the uterus and ovaries.

In treating all types of benign uterine hemorrhage it is well to begin the series soon after complete recovery from the menstrual period. By so doing menstruation is less likely to recur as often after the period as would be the case if the patient were treated immediately before the onset of a period. It makes little difference, however, at what time during the menstrual cycle treatment is begun.

Though it is common for there to be no recurrence of the period, it is also common for the first and second periods to occur; the third period may consist only of a watery, blood-tinged discharge, after which cessation is usually complete.

In establishing a premature menopause in the manner described, it should be stated that the patient does not escape the symptoms which usually accompany this change. It is claimed, however, that the symptoms do not extend over so long a period of time when the menopause is brought on by radiotherapy as when it occurs naturally.

Radiotherapy in the treatment of uterine myoma had its origin in France in 1904. It was not long, however, before the German radiotherapists had adopted a similar treatment by means of the x-ray; however, they advocated much heavier dosage. Controversy soon arose as to the method of action of the rays in curing uterine myoma and its accompanying hemorrhage.

The Germans maintained that the graffian follicles in the ovaries were destroyed and that without maturation of the graffian follicles the ovaries became functionless organs. It was known for some time that an uterine myoma grew smaller and at times disappeared after the menopause and, therefore, the destruction of the ovary, which resulted in the cessation of menstruation, was the cause of the good results obtained by radiotherapy.

The French were equally insistent that the mode of action of the rays was due to a direct effect on the tumor, resulting in a disappearance of its muscular structure.

So far as I am aware, the good results are held to be due to the effect on both the ovaries and the tumor.

Hyperplastic glandular lesions of the endometrium are frequently relieved by curettage, bed rest, and medication. When hemorrhage from the uterus is due to dysfunction of the ductless glands, glandular therapy is indicated.

The response to irradiation in all cases of benign uterine hemorrhage, however, is usually prompt and permanent.

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PLANEOGRAPHY, LOCALIZATION, AND MENSURATION: "STANDARD DEPTH CURVES"

By JULIUS KAUFMAN, M.D., *Brooklyn, N. Y.*

FOR simplicity's sake this treatise has been divided into five sections, as follows:

I. Technical Data.
II. Technical Data Applied to Localization.
III. Technical Data Applied to Planeography.
IV. Clinical Considerations.
V. Summary.

I. TECHNICAL DATA

A roentgenogram of an object may be considered a composite picture of innumerable roentgenograms of parallel, juxtaposed tissue slices of which the object is composed. Thus (Fig. 1), the roentgenogram, $A \ldots B$, really represents a roentgenogram of slice, C–D–E, superimposed upon a roentgenogram of slice, D–E–F–G, etc. If the thickness of the slices be reduced to an infinitesimal quantity, each slice may be considered a plane for all practical purposes. A roentgenogram may be considered, therefore, the integration of serial planeograms. Planeography refers to the differentiation of individual planes.

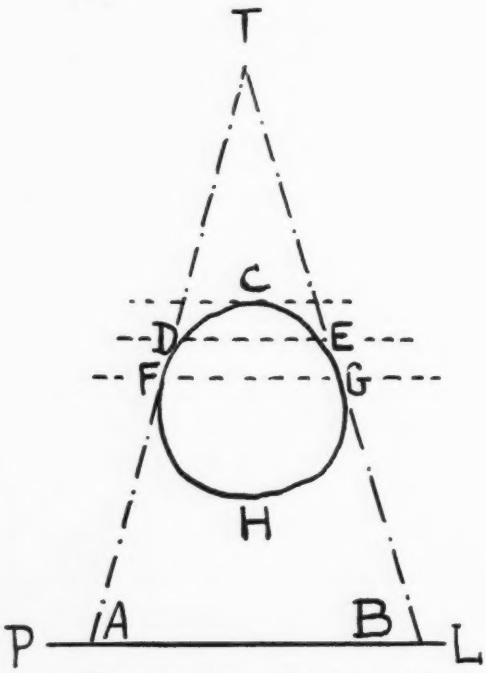
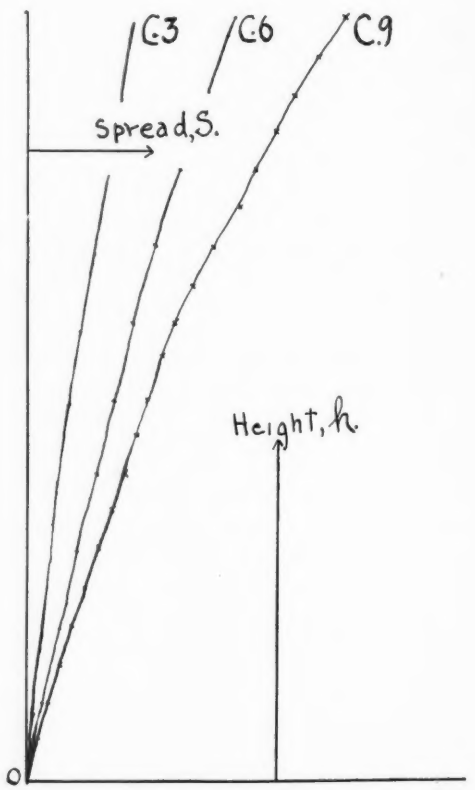


Fig. 1. (T), target position; ($P \ldots L$), plate; ($A \ldots B$), roentgenogram; (C–D–E–F–G–H), object.



Graph I. "Standard Depth Curves": (C.3), height, H, of target above plate = 32 inches; spread of target positions = 3 inches; (C.6), height, H, of target = 32 inches; spread of target = 6 inches; (C.9), height, H, = 32 inches; spread of target = 9 inches.

We have evolved a method by which it is

possible to demonstrate any plane in space, parallel to the plane of the plate, from two (or more) roentgenograms properly taken.

In Figure 2:

(*a*) *C–D–E–F* represents the plane of the plate in the horizontal position;

(*b*) *T.1* and *T.2* represent two target positions, height, *H*, above the plate level;

(*c*) *C–D–G–H* represents a vertical plane, passed through *T.1* . . . , *T.2* intersecting *C–D–E–F* in *X* . . . *Y*.

(*d*) *V.T.2* and *V.T.1* represent the vertical projections of *T.2* and *T.1*, respectively.

(*e*) *A* and *B* represent any two points in a plane parallel to the plane of the plate, height, *h*, above the plate level.

Demonstration:

(1) Pass planes *T.2–A–B* and *T.1–A–B*. They intersect *C–D–E–F* in *T.2.A* . . . *T.2.B* and *T.1.A* . . . *T.1.B*, respectively.

(2) *T.2.A* . . . *T.2.B* and *T.1.A* . . . *T.1.B* are both parallel to *A* . . . *B* and they are, therefore, parallel to each other.

(3) *T.1.A* . . . *T.2.A* and *T.1.B* . . . *T.2.B* are both parallel to *T.2* . . . *T.1* and they are, therefore, parallel to each other, and also to *V.T.2* . . . *V.T.1*.

From the demonstration above the following inferences follow:

(*a*) The images of any, and of all, points in a given plane, parallel to the plane of the plate, exposed in two target positions at the same height above the plate level, move along lines parallel to a line joining the vertical projections of the target positions. In Figure 2, *T.1.A* . . . *T.2.A* and *T.1.B* . . . *T.2.B* are parallel to *V.T.2* . . . *V.T.1*.

(*b*) The spread, *S*, that is, the distance separating the images of a given point, in a given plane in space, is a fixed determinable quantity (*T.1.A* . . . *T.2.A* in Figure 2). Spread, *S*, is equal for all points in that plane (*T.1.A* . . . *T.2.A* is equal to *T.1.B* . . . *T.2.B*).

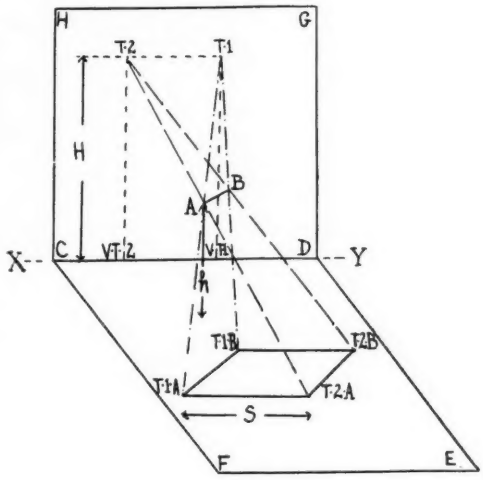


Fig. 2.

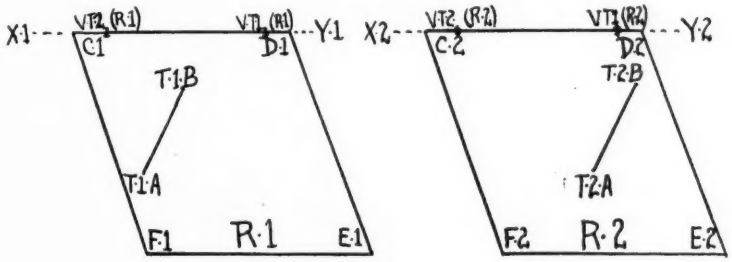


Fig. 3.

(*c*) If the exposures are upon two plates (see Figure 3), *R.1* and *R.2* representing the roentgenograms in *T.1* and *T.2* positions, then *R.2* may be made to superimpose *R.1* exactly (see Figure 4) by superimposing *X.2* . . . *Y.2* upon *X.1* . . . *Y.1* so that *V.T.2*(*R.2*) . . . *V.T.2*(*R.1*) becomes equal to spread, *S*. This superimposition represents the planeogram of the plane in which *A–B* lies (that is, for a plane, height,

h, above the plate level). It can readily be seen that for any other plane in space, spread, S, will vary, depending on its height above the plate level. Since spread, equal to H, the height of the target above the plate level.

Suppose we wish to find spread S, for a point O, height h, above plate level.

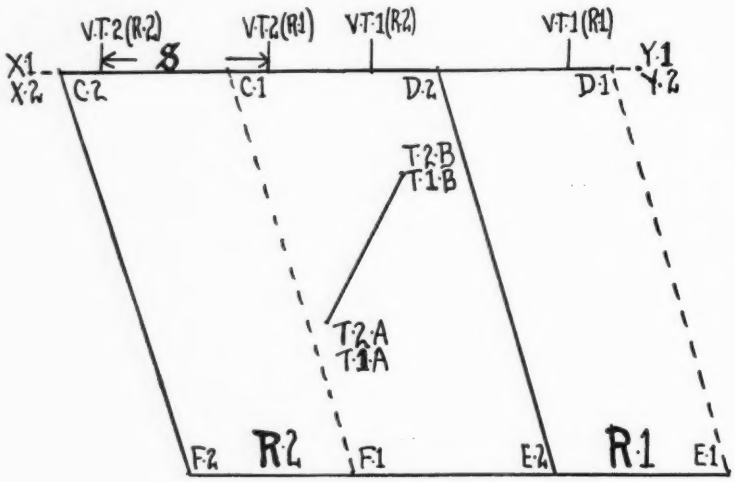


Fig. 4.

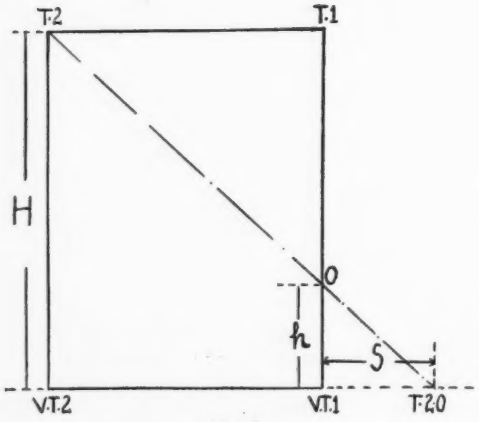


Fig. 5.

S, is the correction factor used in depicting the planeogram, it becomes necessary to determine spread, S, in terms of height level.

The relationship sought may be easily obtained by the following construction (see Figure 5):

Construct (Fig. 5) rectangle *T.2–T.1–V.T.1–V.T.2*, so that *T.2 . . . T.1* is equal to the target shift, and so that *T.2–V.T.2* is

Proceed as follows:

(1) *V.T.1–0* is made equal to h;
(2) *T.2–0–T.2.0* is drawn;
(3) *V.T.1 . . . T.2.0* is equal to spread, S.

If spread, S, is known, height, h, may be found by the reverse construction.

We believe that rectangle *T.2–T.1–V.T.1–V.T.2* is of sufficient importance to be designated by the special name, "the Depth Localization Rectangle," since that is really what it is.

If H is made equal to 32 inches, and *T.2 . . . T.1* to 3, 6, and 9 inches, respectively, three "Standard Depth Curves" can be charted (Graph I), showing the relationships of height, h, to spread, S, under these conditions.

These curves can expeditiously be used in localization and planeographic procedures, provided the plates are taken, using the factors employed in deriving the curves.

These curves we have also designated by the special name "Standard Depth Curves."

II. TECHNICAL DATA APPLIED TO LOCALIZATION

If one wishes to localize a single point, *0*, in space, all that is necessary is to expose it on a single place under standard conditions. The vertical projection, *V.0*, is easily obtained (see Figure 6). The height, *h*, is determined from "the Depth Localization Curve," using *T.2.0* . . . *T.1.0* as spread, *S*.

For localization of a single point, it may be feasible to project both images on a single plate. If, however, information pertaining to complex structures is desired, it is more expedient to make two exposures on two plates, one for each target position. Thus, if point, *0*, were exposed on two plates (see Fig. 7), *7.A* would represent the roentgenogram in *T.1* position, and *7.B* in *T.2* position. The construction (see *7.C* in Figure 7) would then consist of transcribing *7.A* and *7.B* upon the same sheet of paper and proceeding as before (compare *7.C* in Figure 7 with Figure 6).

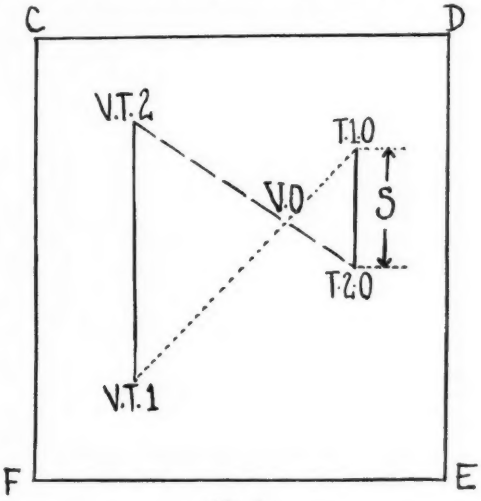


Fig. 6.

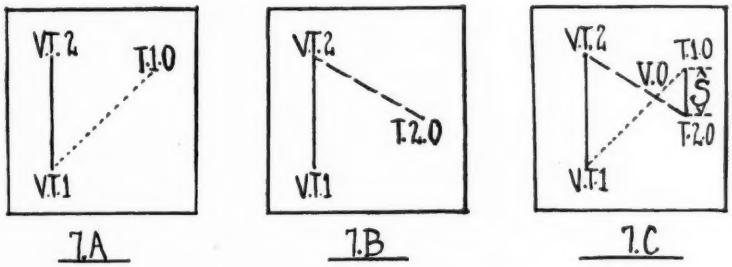


Fig. 7.

If any two given points are localized, it is a simple matter to determine their relationship in space.

Suppose, for example, we wish to determine the distance and obliquity of a line joining the tip of the coccyx to the tip of the anterior superior iliac spine. We first localize these points. From the localization data the information sought may be obtained, as follows:

Expose the pelvis under standard conditions. In Figure 8, *8.A* and *8.B* are schematic representations of such roentgenograms taken in *T.1* and *T.2* positions. The images of the coccygeal tip (*C.1* and *C.2*) are marked on each film. The images of the iliac spine (*S.1* and *S.2*) are similarly marked. These points are transcribed to the same sheet of paper (Fig. 9). Each of the points is localized separately.

The vertical projections, *V.C* and *V.S*, of points *C* and *S* are thus recorded, as are their heights, *h.C* (height of coccyx above plate level), and *h.S* (height of iliac spine above plate level).

The length and obliquity are determined from the data secured by localization as follows:

(1) Draw *V.C* . . . *V.S* (Fig. 10) equal to *V.C* . . . *V.S* (Fig. 9).

(2) Draw *V.C* . . . . *C* perpendicular to *V.C* . . . *V.S*, and equal to *h.C*.

(3) Draw *V.S* . . . *S* perpendicular to *V.C* . . . *V.S*, and equal to *h.S*.

(4) Connect *C* to *S*.

Line *C . . . S* represents the length, and angle *S–C–x* the obliquity.

The above procedures are simple. They constitute all the construction necessary for all localization problems, regardless of their complexity.

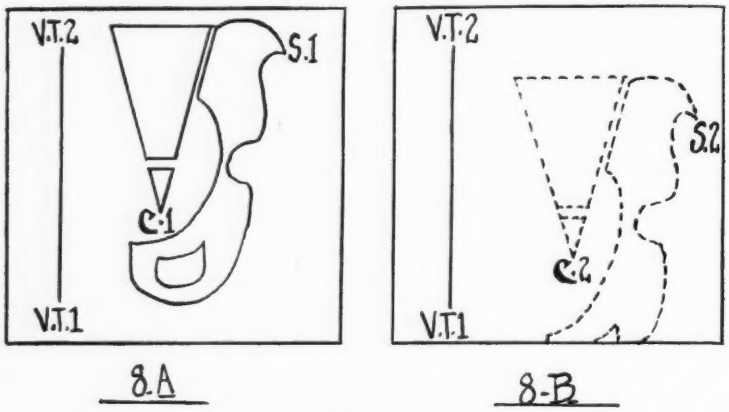


Fig. 8.

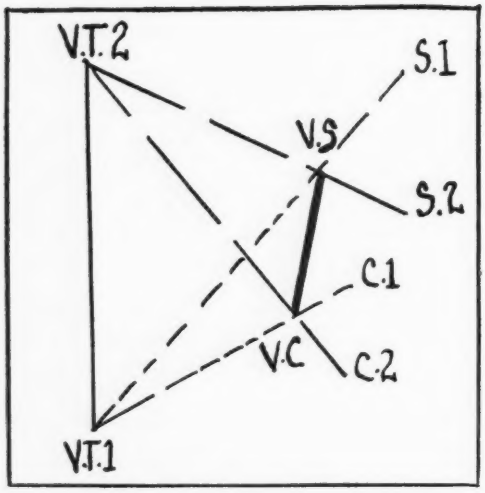


Fig. 9.

III. TECHNICAL DATA APPLIED TO PLANEOGRAPHY

Suppose we wish to determine the planeogram of the pelvic bones for that horizontal plane corresponding to the coccygeal tip. Proceed as follows:

Superimpose *8.A* upon *8.B* so that points *C.2* and *C.1* superimpose. Similar points, one, two, three, four, five, etc., will then superimpose, and they will represent the planeogram sought (see Figure 11).

The height of this plane above the plate level may be obtained from "the Standard Depth Curve," using distance *V.T.1 . . . V.T.1* as spread *S*.

This superimposition of standard roentgenograms for planeographic determinations introduces into roentgenology a new procedure of inestimable value. It not only localizes any given point, but it also defines it, in relation to others in the same horizontal plane.

Furthermore, if one roentgenogram is made to slide upon the other, using the vertical projections, *V.T.2 . . . V.T.1* as an axis, one will be startled by visualizing various planeograms which appear, one a direct continuation of the other, as though one were traversing the actual anatomical structures. If the sliding motion is stopped, an individual planeogram becomes apparent, the height of which, above the plate level, may also be obtained from "the Standard Depth Curve."

IV. CLINICAL CONSIDERATIONS

Planeography may be employed for localization of points, for linear and angular mensuration, but its greatest field of usefulness is apparent when the procedure of "superimposition" of plates is

employed for the determinations of various planeograms. Let us dilate upon this phase more fully.

Suppose there is a calcific shadow in the soft tissues of the bony pelvis and we wish to determine the plane in which it lies. We superimpose the standard plates so that the images of the calcific shadow superimpose. If it should lie in the same horizontal plane as the coccygeal tip, the images representing the coccygeal tip would then superimpose; otherwise they would not. Whichever similar points superimpose, represent the horizontal plane in which the calcific shadows lie.

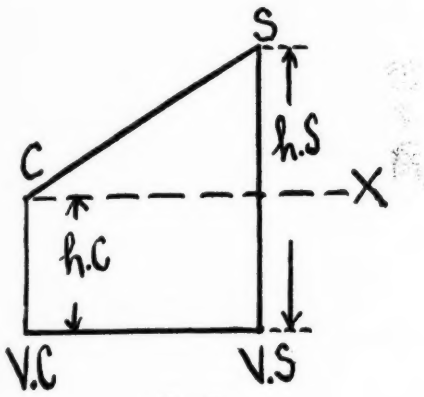


Fig. 10.

Suppose there is a fracture of the skull which appears to involve the sella turcica, and we wish to determine with certainty whether it does or not. We superimpose the images of the sella. If the fracture actually involves the sella, that portion of the fracture in the sella will then superimpose.

If you wish to know whether the anterior superior iliac spines of both sides lie in the same horizontal plane, or whether there is rotation, superimpose the images of one side. If they lie in the same horizontal plane, the images of the opposite side will superimpose.

If one wishes to know whether a calcific shadow lies in the plane of the kidney, planeography may be employed. If numerous calcific shadows are present, it is possible to determine which lie in the plane of the kidney and which do not. We could multiply *ad infinitum* specific instances in which planeography could be em-

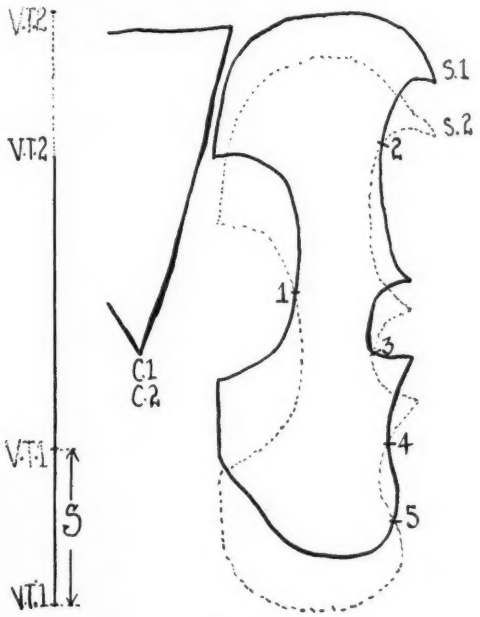


Fig. 11.

ployed. In general, however, it finds its greatest field of applicability in cases in which relationships are essential, as in localization, linear mensuration, angular mensuration, the determination of symmetries and asymmetries, rotations, involvement of structures by pathologic lesions, the determination of structural planes for whatever reason, etc.

V. SUMMARY

In the foregoing treatise, we have demonstrated an original method for the determination of planeograms. In so doing, we have evolved "the Depth Localization Rectangle." We have constructed "Standard Depth Curves," and have demonstrated how they expedite localization. We have correlated planeography and localization. We have finally indicated some of the fields of applicability of planeography in clinical roentgenography.

Just a word about "the Standard Depth Curves." The distance 32 inches was employed for the simple reason that Thoms advises this distance in his method for the determination of pelvic measurements. Three inches was chosen as the spread of the targets for one of the curves, since such plates may also be viewed stereoscopically.

We believe it is imperative that the factors employed in localization be standardized and that depth curves be prepared under such conditions. We believe that these curves should be a part of every roentgen laboratory just as charts for cardiac measurements are. In all other radiographic procedures, standard routine measures are employed. We see no reason why there should not be a "standard routine localization" procedure, in which "standard depth curves" are used for depth determinations. Localization could then be made practical and simple. The taking of the plates and the charting could then be done by practically anyone, whether or not he possessed mathematical training. From the standard plates taken for localization, planeograms could at the same time be made.

Finally, we wish to state that planeography opens new fields in research. This we have not touched upon, but we hope to report upon this phase at a later date, providing, of course, such research bears fruit.

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THE EFFECT OF THE X-RAYS UPON THE FINE STRUCTURE OF THE PARENCHYMA OF THE THYROID GLAND

(SECOND ARTICLE)

By PROFESSOR B. S. ZIMNITSKY, DR. N. A. BASKINA, *and* DR. A. P. DEVIRZ, of the Experimental Biological Department of the Ural Roentgenological Institute, *Svordlovsk, U. S. S. R.*

IN the preceding article[1] we discussed the action of x-rays in relation to the fine structural changes that are developed in the parenchyma of the normal thyroid gland. It would seem that the study of the results produced by this treatment upon the thyroid gland in the state of hypersecretion must surely be of greater interest. While in the clinic the x-ray is used as a therapeutic agent for the treatment of Basedow's disease, yet in the literature at our disposal we do not find any description of experimental morphologic investigations. We know that the laws applied to normal conditions cannot always be applied to pathologic processes and *vice versa*.

In the present investigation we want to solve the following problems:

(1) Whether the parenchyma of the thyroid is able to increase its secretory activity after partial thyroidectomy, *e.g.*, to give the compensatory hypertrophy, if this gland has undergone preliminary x-ray treatment.

(2) Whether the compensatory hypertrophy will develop after partial thyroidectomy, if the organ is radiated immediately after the operation or after a lapse of time.

EXPERIMENTS AND METHODS

Rabbits were used for the experiments just as in the first case. In the first lot of rabbits for our present experiments the region of the thyroid was radiated with from 5 to 10 H.E.D., using 1 H.E.D. per day. (For the method of radiation, see Article I.) Immediately after the radiation or from 5 to 10 days later complete extirpation of the thyroid from one side was performed. This gland served as control No. 1. Then in 20, 30, and 40 days, respectively, the rabbits were killed and the thyroid on the other side was removed and was used as the experimental gland. While this was being done to the experimental rabbit the normal rabbit was operated upon and killed. The thyroid removed before killing served as control No. 2 and the thyroid from the other side removed after killing served as control No. 3. The second series of experiments was performed as follows: The thyroid control No. 1 of the normal rabbit was extirpated from one side. After the operation (usually from the third to fifth day), radiation of the animal was begun, giving 10 doses for from 15 to 20 days. The animals were killed just after the last radiation, or from 10 to 15 days later. The gland then removed was taken as the experimental gland. The other animals were operated upon in the same way; the extirpated gland was taken as control No. 1 and 20 days later the other was radiated, receiving 10 doses during 15 days. Some animals were killed directly after the last radiation, the others 10 days later. The thyroid then removed was taken as the experimental gland. Simultaneously the control rabbit was operated upon, its extirpated gland served as control No. 2, and then it was killed. The thyroid removed after killing was control No. 3.

For the first series we used five experimental and five control rabbits; for the second series, eight experimental and six controls. The method of making the preparations was the same as described in the first article.

[1] RADIOLOGY, July, 1936, **27**, 68–74.

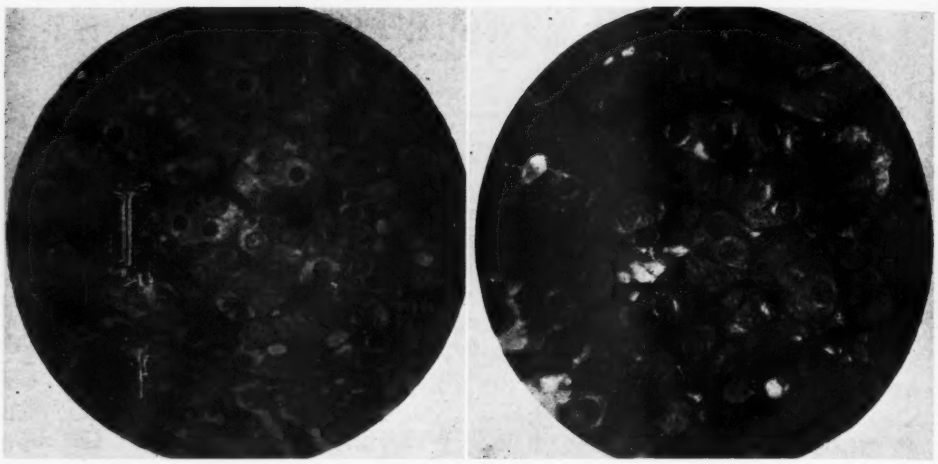

Fig. 1. (Experiment 4.) The thyroid gland control No. 1. Staining for chondrioma by Kull's method. The magnification for all photomicrographs is the same.
Fig. 2. (Experiment 4.) The experimental thyroid gland. Staining by Kull's method.

OUR FINDINGS

First we shall speak about the first series of our experiments in which the radiation of the thyroid was done preliminary to partial thyroidectomy. We shall describe only one of the most typical experiments, because all of the experiments gave more or less the same morphologic data.

Experiment No. 4.—A rabbit, weighing 2,300 grams, was treated 15 days and received 10 H.E.D. Its thyroid from one side was completely extirpated, 10 days after the last radiation (Control No. 1).

Histologic examination of this gland (Fig. 1) shows it to consist completely of comparatively small follicles with diameters of from 5 to 32 microns; the epithelium of the follicles is of a low columnar or cuboidal shape, the height of its cells being from 5 to 8 microns; its nuclei are round, vesicle-shaped, their dimensions averaging 5.5 microns. Often the pycnotic nuclei are found in the epithelium. Chondrioma in the cells of the epithelium is rough and its regular disposition in a cell-body is lost. The lumina in most of the glandular vesicles seem empty because colloid lies in the form of a small clot upon the walls of the follicles thereby freeing the lumina of the follicles. In the individual follicles, which are filled with colloid, the colloid is penetrated with large vacuoles. Thirty days after the thyroidectomy the remaining thyroid was extirpated and it served as the experimental gland.

EXAMINATION OF THE EXPERIMENTAL GLAND

The examination of the experimental gland (Fig. 2) shows that it consists of follicles with diameters of from 8 to 32 microns. The follicular epithelium is of columnar and high-columnar shape and its cells are of large dimensions, having a height of from 13 to 16 microns. The nuclei in them are very large, being from 6.5 to 8 microns. Chondrioma in the epithelium of a gland is very robustly developed. It abounds in the cell-body and has a normal distribution, massing especially at the apical pole and along the border with the colloid.

In general, it is necessary to stress that in the present experiment chondrioma is more strongly developed than in the glands of the normal control animals. The lumina of glandular vesicles usually are empty and collapsed. Sometimes they are filled with a fine granular mass of colloid

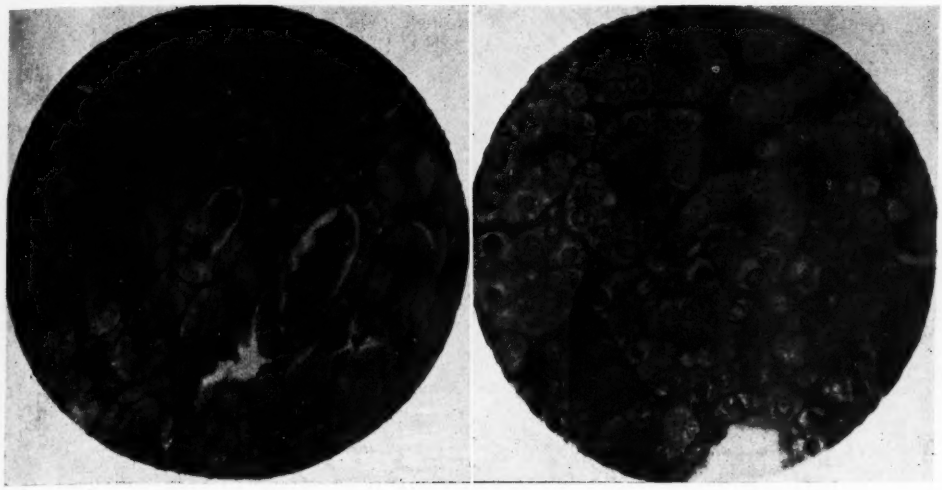

Fig. 3. (Experiment 4.) The thyroid gland control No. 2. Staining by Kull's method.
Fig. 4. (Experiment 4.) The thyroid gland control No. 3. Staining by Kull's method.

which in some places lies in the form of a fine nuclear net.

The Control Rabbit.—Male, weighing 2,980 grams; operation, partial thyroidectomy, the thyroid (control No. 2) being completely removed from one side. Thirty days later the other thyroid (control No. 3) was extirpated.

The histologic examination (Fig. 3) shows that the gland (control No. 2) is of normal structure; that is, the diameters of its follicles are from 16 to 48 microns. The epithelium of the follicle is of a cuboidal and sometimes columnar shape, being from 6.5 to 9.5 microns high. The sizes of the nuclei in it are from 5 to 6 microns. Chondrioma in the form of fine little sticks is regularly spread in the cell-body, often gathering more thickly at the apical poles of cells. Follicles are filled with homogeneous colloid, penetrated in some places with vacuoles.

The control gland No. 3 (Fig. 4) presents quite a different picture. Its follicles are not large in size, their diameter being from 16 to 38 microns. They are lined with epithelium, the cells of which are very large, columnar or high columnar in shape and with a height of from 6.5 to 11 microns. Their nuclei are 6.5 microns. Often the apex of these cells intrude like a dome into the lumen of the follicle, so that the apical poles of the cells of the epithelium appears like the top ridge of a fence. Chondrioma is very richly developed in the cells and is disposed regularly in the form of thickly massed grains, collected expecially at the apical poles. The lumina of the follicles are either hollow and collapsed or filled with thickly vacuolated colloid.

Now we come to the description of the second series of our experiments in which the thryoid, left after partial thyroidectomy, was treated by x-rays. We shall describe here also only one experiment, because the data obtained from the various experiments were quite analogous.

Experiment No. 7.—A male rabbit, weighing 2,620 grams. The operation consisted of the complete removal of the thyroid (control No. 1) from one side; 20 days later the other thyroid was treated for 15 days and received ten doses. The day following the final radiation, the rabbit was killed and the other gland (experimental gland) was removed.

The Morphologic Examination.—The examination of the gland (control No. 1) showed the usual normal structure, but the

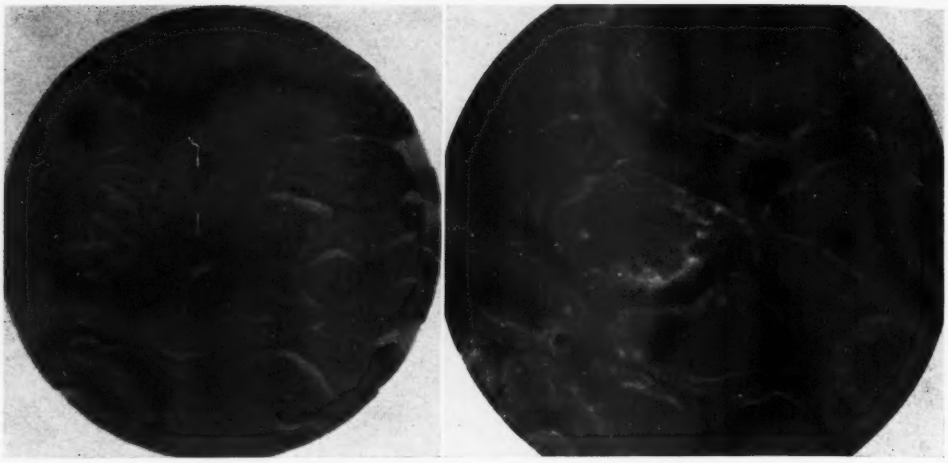

Fig. 5. (Experiment 7.) The thyroid gland control No. 1. Staining by Kull's method.
Fig. 6. (Experiment 7.) The experimental thyroid gland. Staining by Kull's method.

examination of the experimental gland (Fig. 5) showed the following picture. Its follicles were decidedly enlarged in size in comparison with the follicles in the control gland, most of them being 58 microns in diameter. The follicular epithelium was of cuboidal or low cuboidal shape and reached a height of from 3.2 to 6 microns. Its largest nuclei were 5.5 microns.

There was a small amount of chondrioma in the cells, especially in the low flattened cell elements. The follicles with the higher epithelium were richer with chondrioma. The follicles were filled with a homogeneous mass of colloid which in some places was vacuolated. It seems important to point out that the organ had increased its colloid content considerably; the follicles had been enlarged in size and there had been a decided flattening of their epithelium. Chondrioma was poorly developed in the cells. We wish to stress the fact that in the present gland we found almost no pycnotic nuclei.

In the control rabbit we removed the thyroid (control No. 2) from one side and 35 days later removed the thyroid (control No. 3) from the other side. The structure of the thyroid control No. 3 was analogous with the control No. 3 of the first series of the present article.

DISCUSSION OF THE FOREGOING FINDINGS

The interpretation of the foregoing findings presents no special difficulty. In the series of experiments with preliminary radiation of the thyroid before partial thyroidectomy, we find the following condition. The cells of the thyroid treated by x-rays partially degenerate, as is seen from our first article. Some of the deteriorated cells, when the radiation is stopped begin to reconstruct their structure little by little (see first article). The gland control No. 1 shows just such a transitory condition. What do we find in the experimental gland which has undergone preliminary x-ray treatment and then, because of removal of the thyroid gland from the other side of the neck, was brought to the condition of having to supply increased secretion to the organism? Its morphologic examination thirty days after this operation shows that the epithelium of the follicle was changed from a cuboidal and low columnar form into a columnar and high columnar epithelium. The nuclei in the cells became larger. Chondrioma became extremely abundant and presented quite a normal appearance. The amount of chondrioma in the cells was found to be more abundant than in those of the normal

rabbits. It shows that the cells of a gland undergo quite the same process of hypertrophy as previously described after partial thyroidectomy by the investigators Beresovsky, Breisacher, Trautmann, Halsted, Lasovsky, Wagner, Wieker, de Ligneris, Marins, Tchasovnicov, Zimnitsky, and Zatvornitskaya and this coincides with what we found in the normal rabbit operated on in the same manner (see control No. 3). What does this indicate? There is no doubt but that it indicates increased secretory work on the part of the gland. The observations by Tchasovnicov, Anderson, Schmied, Galeotti, Trautmann, Isenschmid, de Quervain, Wegelin, and others prove that the larger the cell of the epithelium of the follicle, the stronger its function and *vice versa;* the low flattened epithelium in the glandular vesicles indicates a decreased activity of the gland. The observation of Georgievsky, Koijma, Herring, Sirnev, Klivanskaja and Krol, Garnier, Lenhard, Langhaus, and others on feeding animals with a thyroid gland show that the follicular cells of the thyroid of animals so fed become very low, because the organ is brought to a condition requiring less secretion from its organism, due to the outside introduction of this secretion. Yet the extremely abundant chondrioma in the cells indicates the increased secretory activity of these cells. Now we come to the explanation of the phenomenon of the decrease of colloid content in the follicles of both the experimental and control rabbits after thyroidectomy. This decrease is sometimes so pronounced that the lumina of many glandular vesicles seem empty and as if collapsed.

Wegelin and Krause have already pointed out that the amount of colloid in the follicles of a gland represents on one hand a function of the secretory work of the epithelium of the follicles and, on the other, the result of the ejection of colloid from the glandular vesicles into the blood stream. Due to partial thyroidectomy and because of the insistent requirement for secretion on the part of the organism, there is present such a great elimination of the secretion from the lumina of the glandular vesicles into the blood that even the secretory cells of the follicles which underwent hypertrophy fail to fill the follicles with their secretion. Thus our experiments showed that the treated thyroid proved to be able not only to rebuild its structure up to normal, but, because of the increased demand on the part of the organism for greater activity, the thyroid responded with an increase of its incretion as well as with the phenomena of a compensatory hypertrophy. But if after the same lapse of time after partial thyroidectomy we compare the radiated gland with the thyroid of a control (see in the first series of experiments, the experimental gland and control No. 3), it is quite evident that the phenomena of compensatory hypertrophy of the control thyroid is much more pronounced. Evidently this can be explained by the fact that the cells of the radiated thyroid have to rebuild their normal structure and then, in consequence of the trauma produced by the treatment, to increase their secretory power. Therefore, it is more difficult for them than for the cells of a normal gland.

Now let us discuss the second series of experiments. The thyroid after partial thyroidectomy was radiated while the organism had made an increased demand for secretion. Our findings demonstrate that in the thyroid of the experimental rabbit not only the phenomena of compensatory hypertrophy and increased secretion are not developed, but there was even a decrease of the function of the organ and a retention of colloid. The following morphologic data prove this; the decrease in the height of the cells of the follicular epithelium; the decrease in the diameter of its nuclei and the impoverishment of chondrioma in the cells. According to Anderson, Schmied, Galeotti, Müller, Trautmann, Isenschmid, de Quervain, Wegelin, Tchasovnicov, and others, this condition of the cells indicates their decreased secretory activity. We see that the diameters of the glandular vesicles are very

large because of the abundance of colloid. We cannot blame the superabundance of colloid in the gland upon increased production, since the secretion is decidedly decreased; therefore, it may be due to its retention in the organ. But this does not agree with the fact that there is an increased requirement for the secretion on the part of the organism.

The secretion should have been eliminated quickly in the most active way (see control No. 3, obtained by partial thyroidectomy of a normal rabbit).

Therefore, we do not understand the reason for the retention of colloid and we cannot offer any satisfactory explanation. Thus the x-ray suppresses the necessity of cell elements to increase their secretion and their compensatory hypertrophy, which should have developed in them after partial thyroidectomy (see controls No. 2 and 3). On the contrary, they create the phenomena of a decrease of function and the retention of colloid in the organ. Here it will be well to draw attention to the extremely interesting fact that, as a rule, the x-rays produce almost no phenomena of degeneration in the cells of glands of experimental animals. In the normal thyroid of radiated animals we observed the pycnosis of nuclei, vacuolization of protoplasm, and degenerative changes in chondrioma. But in our experiments with radiation of the thyroid, after partial thyroidectomy the phenomena of degeneration were almost entirely absent. It seems as if the x-rays in these experiments acted chiefly quantitatively and not qualitatively upon the morphologic condition of the cells. The conclusion intrudes that the effect of x-rays upon the cell is not always the same, and depends upon the functional condition of the cell. On the basis of both of our articles we arrive at the following conclusion: the parenchyma of the thyroid is rather resistant to the x-rays. Their effect upon the cell of the thyroid is not the same, but depends upon the condition of the cell. In general, the x-ray action oppresses the secretory process in the thyroid and provokes a degeneration of the cells and the disintegration of a part of them. The degree of intensity of the depression of the functions and the phenomena of degeneration is in direct proportion to the dosage. The normal thyroid, having gone through a certain amount of degeneration and a decay of a part of its cell-elements, is able to re-establish morphologically its functions, after a lapse of time, approaching the normal. Even more, large doses of x-rays, which kill a considerable amount of cell-elements in the organ, later can provoke a compensatory increased secretion in the remaining cells and also their hypertrophy.

The effect of large x-ray doses corresponds to partial thyroidectomy. The x-rays are also able to arrest the development of the compensatory hypertrophy, which should take place in the cells of the gland after partial thyroidectomy. Further, because of the disintegration of degenerated cells and of the undoubted influence of x-rays upon the structure of colloid in the gland, a condition in the organism may be produced after radiation in which the products of degeneration and colloid are increasingly passed into the blood; that is, a hyperhormonization of the organism is created in the early days after radiation. On this basis we feel free to assume that the use of x-rays for the treatment of the diseases of the thyroid, particularly of Basedow's disease, is not a simple procedure. First, the dosage should be in direct proportion to the strength of hypersecretion of the organ. Further, the given doses always—and especially at the beginning of the treatment—may provoke increasingly auto-intoxication because of the increased absorption of the products of degeneration of the gland cell-elements. X-rays, acting on the "island principle" and depending upon the strength of the dose and the resistance of the cells, also the variation of time after radiation, may bring about the phenomena of steady hypofunction of the organ or may redevelop the phenomena of Basedowism. All this proves that x-ray therapy of

Basedow's disease requires strict objective methods of control (*e.g.*, the metabolimetry, the determination of the tone of the vegetative nervous system, the determination of the blood picture, Kottmann's reaction, etc.) over the function of this organ during radiation as well as for a considerable time thereafter. In addition to this, it is necessary to take into account the possibility of toxicosis at the beginning of the treatment.

CONCLUSIONS

1. Cells of the normal thyroid treated by x-ray are not only able to re-establish their functions up to the normal, but under radiation, which acts upon them in a manner similar to a partial thyroidectomy, may bring about the phenomena of compensatory hypertrophy and also hypersecretion in the remaining intact cells.

2. The x-rays having been used for the treatment of the thyroid of a normal animal, after partial thyroidectomy, that is, during the time of the more intensely functioning cell-elements, may stop the development of their compensatory hypertrophy and hypersecretion and may even decrease the activity of the cells below the normal.

The x-ray treatment of Basedow's disease should be strictly individual for each case and it should be obligatory that it be carried on under the control of the objective methods for determining the functions of the thyroid during the time of treatment and for a considerable time thereafter.

At the beginning of the treatment it is necessary to pay strict attention to the phenomena of increased auto-intoxication.

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FRACTURES OF THE SPINE

REPORT OF 173 CASES

By ROY G. GILES, A.B., M.D., *Temple, Texas*

From the Department of Roentgenology, Scott and White Clinic

ROENTGENOLOGIC consideration of the spine has established the presence of a large group of congenital anomalies and defects. Added to these normal differences there is the influence of disease, including the various hypertrophic changes resulting from age, posture, and occupation. Structural changes may also give rise to a confusing picture, which may be difficult to differentiate from fracture. These anatomic variations are often complicated in the same spine by traumatic and non-traumatic lesions, or accompanied by the presence of pathologic conditions which may be attributed to trauma or other causes. Experience has shown that this complexity of conditions gives rise to a vertebra that is not entirely constant in appearance.

Congenital anomalies are rare in the cervical and dorsal regions but extremely common in the lumbar and lumbosacral segments. In 1931, the writer reviewed 1,122 consecutive genito-urinary examinations and found 38.7 per cent of anatomic variations in the lumbar and lumbo-sacral segments. Bohart and Cushway and Maier made a routine x-ray examination of all individuals entering the employment of the Belt Railway Company of Chicago, and found that approximately 44 per cent of 1,000 symptomless spines revealed some type of anomaly. *Spina bifida occulta* was the most frequent variation noted, and sacralization was the next in frequency. The above mentioned authors concluded that anatomic variations do not predispose to prolonged disability or increased tendency to injury unless accompanied by hypertrophic changes. The importance of these anatomic variations should not be over-emphasized, but familiarity with them is necessary in order to avoid error in mistaking these congenital defects for fracture.

The following tabulation shows the level of involvement in a series of 173 cases of fractured vertebræ observed in the x-ray department of the Scott and White Clinic, and the Gulf, Colorado and Santa Fe Hospital, during the past ten years.

	Scott and White Clinic	G., C. and S. F.
Sacrum	12 cases	2 cases
Transverse processes	15 cases	4 cases
Cervical vertebræ	11 cases	3 cases
Dorsal vertebræ	25 cases	5 cases
Lumbar vertebræ	44 cases	13 cases
Dorso-lumbar vertebræ	35 cases	4 cases
Total	142 cases	31 cases

Anatomically, the spine consists of 33 segments. In the adult, nine of these are fixed, composing the sacrum and coccyx.

Further discussion will be limited to a consideration of fractures of the presacral or movable vertebræ and, briefly, their differential diagnosis.

The following tabulation shows the distribution of the 201 fractured bodies in 140 cases, averaging 1.4 segment to the case.

	Cervical	Dorsal	Lumbar
First	1	1	50
Second	2	0	26
Third	0	1	9
Fourth	1	1	11
Fifth	7	1	5
Sixth	8	5	
Seventh	1	5	
Eighth		6	
Ninth		6	
Tenth		11	
Eleventh		14	
Twelfth		29	
	20	80	101

The most common site of fractures in this series of cases was in the dorso-lumbar region. Forty-two (37 per cent) of the 115 cases observed in the Scott and White Clinic were women, and 73 (63 per cent) were men. Ninety-three of the 140 presacral cases revealed fractures of single segments: five cervical, 31 dorsal, and 57 lumbar. The remaining 47 cases presented multiple fractures. Eight of the cases of fracture in the cervical region presented 17

fractured segments. The 39 cases of multiple fractures in the dorso-lumbar region revealed 91 fractured segments, with associated dislocation in 14 cases.

The 19 cases of fractured transverse processes showed involvement of 37 transverse processes. Seven cases were associated with fractures of the vertebræ, and three of the transverse processes of the fifth lumbar were associated with fractures of the sacrum.

The tabulation below shows the etiology in 78 (68 per cent) of the 115 cases of presacral vertebræ observed in the Scott and White Clinic:

Automobile accident	42 cases
Falling from a height	22 "
Diving	5 "
Injured by train	4 "
Horse-drawn vehicle	3 "
Aeroplane crash	2 "
	78 cases

The tabulation below shows the occupation of the 29 cases with fractures of the presacral region observed at the Santa Fe Hospital:

	Cases	Duty	Cause of "Off-duty" Injury	Old Fracture	Paralysis
Laborer	7	7	0	0	3
Switchman	6	5	Struck by speeding car	0	2
Brakeman	4	4	0	0	1
Engineer	3	0	Elevator cable broke		
			Fell off ladder	2	1
Conductor	2	?	?	2	1
Machinist-helper	1		?	1	0
Coppersmith	1	1	0	0	1
Boilermaker	1	0	Car accident	0	0
Draftsman	1	0	Football, 1922	1	0
Signal helper	1	1	0	0	0
Clerk	1	0	Motorcycle	0	0
Stenographer	1	0	Riding in car	0	0
Total	29	18	7	6	9

The most common injury to the spine is a compression fracture of the body. According to Albee, this injury constitutes about 80 per cent of vertebral fractures. Spinal fractures are usually simple but may be compound. The etiologic factor is a direct or indirect force applied to either end of the spine, resulting in hyperflexion or hyperextension of the spinal column.

Fractures in which there is a demonstrable injury to the spinal cord may show transitory or complete paralysis. Many patients so paralyzed may respond to careful, conservative treatment, while others are hopeless from the very start. When the cord is severely torn or crushed, only slight improvement is to be expected, because the cord tissue has little power to regenerate.

A much larger and more important group of cases is that in which no signs of cord lesion can be elicited. Such fractures may involve either the accessory portion of the vertebra or the body itself. Statistics regarding the exact percentage of vertebral fractures occurring with and without cord symptoms are rare. In 1925, Sherwood Moore wrote: "Since 1911 there have been observed in the Roentgen Department of Washington University 69 fractures of the spine, about 3 per cent of all fractures observed during the same period. Of the total number of cases, 21 (30 per cent) were acute, with a classical picture of fracture; 48 cases were adventitious discoveries." Forty-four (31 per cent) of the 140 cases of fractures of the bodies of the presacral vertebræ observed in our series presented the classical symptoms of fracture.

Due to the fact that only a comparatively small percentage of cases of fractures of the spine has been proved by laboratory findings, operations, or postmortem examinations, it seems safe to assume that vertebral fractures heal in the same manner as fractures elsewhere; that is, fractures of the vertebræ almost immediately undergo a process of repair and callus formation. The body of the vertebra at first is comparatively soft and may undergo a process of rarefaction or attrition, being readily compressed further before the callus has had time to consolidate. Unless proper treatment is instituted, and the injured vertebra protected for a long time, there may be, after several weeks or months of weight bearing, increased deformity, accompanied by pain and weakness in the

spine, and neuralgic and motor disturbances in the legs.

There remains to be discussed Kümmell's disease, a condition first described in 1895 as non-tuberculous osteitis of the vertebral bodies, accompanied by softening and collapse of a body. The literature has been well reviewed in recent papers by Baker, Blaine, Jones, and Kümmell. The exact nature of the condition is perhaps not well understood and there remains a great deal of doubt and confusion. Osgood and Steindler believe there is no doubt of the existence of the condition as a clinical entity. On the other hand, O'Brien, George and Leonard, and other authorities express considerable doubt as to the occurrence of any such process as Kümmell described, and suggest that many of the cases are unrecognized fractures of the spine.

A careful perusal of the case reports indicates the possibility of many of these cases being simply small, unrecognized fractures of the spine with delayed symptoms. Unquestionably many of the reports of so-called Kümmell's disease are simply delayed symptoms following an unrecognized fracture of the spine. A diagnosis of Kümmell's disease is hardly justified unless a careful x-ray examination immediately after the injury is negative and is followed later by positive findings in the roentgenogram. No doubt, there are authentic cases in which the criteria set forth for the diagnosis of Kümmell's disease are fulfilled: at the same time we must bear in mind that this disease entity is extremely uncommon.

Fracture of the spine must be differentiated from metastasis, tuberculosis, osteomyelitis, syphilis, old hypertrophic arthritis, and the natural collapse of the bodies of the vertebræ with excessive calcium absorption in old age.

Metastatic lesions are nearly always carcinomatous, although Hodgkin's disease may be encountered. The rather rare osteoblastic type of secondary malignancy may produce a marble-like bone of great density, usually without the occurrence of wedge-shaped vertebræ. The most frequent destructive or osteoclastic type usually produces irregular, moth-eaten areas of destruction. The intervertebral discs are destroyed, whereas in fracture they remain intact. Tuberculosis and osteomyelitis are recognized on the roentgenogram by bone destruction and narrowing of the intervertebral discs. The vertebra becomes wedgeshaped, this condition being more marked in tuberculosis. In tuberculosis there are rarely bone proliferation and callus formation, whereas in osteomyelitis these changes are present. The history of the case and the absence of trauma are important factors in the establishing of a diagnosis of osteomyelitis and Pott's disease. Syphilis, on the other hand, is usually accompanied by extensive new bone formation, and the extent of the lesion is more marked than the symptoms would indicate. Osteoarthritis, or spondylitis, often presents great difficulty in diagnosis, especially if the injury producing the alleged fracture is of several months' duration. The new bone in spondylitis is in the form of spurlike formations and is laid down along the margins of the vertebræ in the form of a fringe, which may later bridge across and fuse. Frequently there is absorption of the lime salts from the body of the vertebræ in the senile, giving rise to a gradual collapse of the bodies. This produces a kyphosis, which presents a smooth, rounded curve of the bodies of the vertebræ, differing from the irregular angulation in fracture of the spine.

The diagnosis of fracture of the spine is readily associated with severe trauma and the classical symptoms accompanying these fractures. It must be remembered that a very slight trauma may cause a fracture or dislocation of the vertebræ. Many vertebral fractures in which there is no demonstrable injury to the spinal cord are overlooked, simply because their immediate symptoms do not seem to be of sufficient gravity to suggest a fracture. Nevertheless a history suggestive of fracture may be obtained from many patients who have had osteo-arthritis, aggravated by injury. Similar mistakes may occur in connection with osteomyelitis and Pott's disease.

The physical examination should be made as complete as possible because many of the physical signs may be overlooked, only to show up on a later examination, thus deceiving the examining physician or leading him to believe that a progressive lesion is present. The physician or surgeon can give satisfactory directions for the x-ray investigation of a sufficient area of the spine only after a careful and thorough physical examination.

The final diagnosis must often depend on the roentgenogram. The number of unrecognized fractures of the spine can be reduced to a minimum with the aid of adequate x-ray technic and painstaking interpretation of the roentgenograms, based on anatomic and pathologic facts. Roentgenograms taken in the anteroposterior and lateral planes will furnish the most convincing evidence of vertebral fractures. A good lateral view will not infrequently be the deciding factor.

It is well to remember that a disabling fracture of the spine may be the result of a seemingly simple or trivial accident. Many cases of compression fractures of the vertebræ without classical symptoms may recover with little treatment, but it is useless to assume that all will do so. Only the routine x-ray examination will prevent frequent error in the handling of back-injuries. Routine x-ray examinations in every case of spinal injury will at times show a lesion that cannot be positively demonstrated in any other way.

SUMMARY

Fractures of the spine are quite common, comprising 6 per cent of the total number of fractures observed in the Scott and White Clinic over a ten-year period.

Anatomic variations, because of their frequent occurrence, deserve special consideration in the examination of vertebral injuries. They should not be over-emphasized but should be recognized and reported, in order to avoid error.

Every case of spinal injury should have the advantage of a careful x-ray examination.

The early recognition of spinal fractures is too frequently overlooked. This may be due to inadequate history and physical examination or to insufficient x-ray study, the latter including poor technic, failure to examine a sufficient area of the spine, or the omission of lateral views.

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SOME PHYSICAL PROBLEMS OF HIGH VOLTAGE X-RAY THERAPY[1]

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A NUMBER of physical problems must be solved before the dosage of x-rays produced at voltages from 400 to 1,000 kv. can be placed on a basis as definite as the present system of 200 kv. therapy. Some of these questions will be outlined and briefly discussed under headings dealing with the requirements of the biologist working with narrow beams and small test objects, and of the therapist irradiating tissues at a depth.

When living cells are exposed to x-rays of sufficient intensity, injury to the cells results. The problem of therapy is to administer this destructive agent with the most benefit and the least damage to the patient, for there is always damage.

The part of the physicist in this task is to analyze and control the physical factors involved in an exposure to x-rays in order to provide a reproducible and systematically variable range of conditions of irradiation. These conditions can then be correlated by the biologist with his observations on the effects produced in individual cells and isolated tissues, and finally by the clinician with the therapeutic results obtained with patients.

In the time allotted it will, of course, be impossible to attempt a detailed technical discussion of the announced subject; instead, my aim will be to indicate in a general way the extent to which the physicist is at present able to extend to the high voltage range the system of dosage which he has developed for voltages up to 200 kilovolts.

SYSTEM OF DOSAGE IN USE FOR 200 KV. THERAPY

With regard to the effect of irradiation on a small test object, such as a single cell or a small particle of tissue, the relevant physical factors may be distinguished as (1) rate of production of kinetic energy of high speed ionizing electrons in unit volume per second, (2) duration of exposure, and (3) wave length of the absorbed radiation.

No satisfactory experimental method having been found for measuring directly either the energy of secondary electrons or the amount of ionization produced in tissue or fluids, the production of ionization in a gas was adopted as a basis of dosage. Thus, the intensity of irradiation of a small test object exposed to a beam of x-rays is specified by stating the ionizing effectiveness of the beam in free air as expressed in roentgens per minute and measured in a standard open air ionization chamber or with a calibrated thimble chamber.

For the specification of wave length, direct and indirect methods have been provided which are adequate, if not always convenient.

Using the physical basis of dosage here outlined, the study of small biologic test objects has shown that the response of such objects to an exposure measured in roentgens may be regarded, at least to a first approximation, as independent of wave length up to 200 kv. and higher.

In what has been said so far, we have been thinking about the needs of the biologist in his attempt to correlate exposure conditions with the biologic effect on cells or small particles of tissue which can be exposed directly to the source of radiation. We now come to the more difficult problem presented by the therapist who wants a set of reproducible exposure factors with which to correlate his results when irradiated cells are located in a large mass of absorbing material exposed to a wide beam. Here

[1] Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, at Detroit, Dec. 2–6, 1935.

neither the quantity nor the quality of the dose received by the tissue, which it is desired to influence, bears any simple relation to the dose administered to the patient. This is because the tissue receives a large part of its effect from energy scattered by the surrounding tissues, which may be degraded to much longer wave lengths by the scattering process.

The problem is simplified by the wave length independence of the response of small test objects, which restricts the importance of wave length to the question of penetration.

Since the dose inside the body cannot be measured directly by means of the standard open chamber, recourse has been had to thimble type chambers. Even these cannot be used with the living patient except on the surface or within the mouth, rectum, or vagina, so that it is necessary to fall back on measurements in water phantoms or, preferably, cadavers. This method is not ideal, for it is difficult to be sure that the radiation at a depth does not include wave lengths longer than those for which the chamber is calibrated. Also, such chambers are necessarily so large that it is impossible to place them in such a way as to be sure of always measuring properly the dose received by the cells of the skin. And the skin dose is important because of legal complications.

Because of the difficulty of specifying intensities inside the human body, it is still common practice to correlate clinical results for specific parts of the body with the external exposure conditions, namely, intensity measured in air, voltage, filtration, skin-target distance, area of portal, etc. Water phantom data then serve as a rough guide to the intensity changes to be expected when the external conditions are changed.

REQUIREMENTS FOR DOSAGE AT 1,000 KILOVOLTS

The distance travelled by the ionizing secondary electrons increases rapidly with the voltage of the x-rays by which they are produced and becomes large as compared to the size of a cell. As a result, if small test objects such as *Ascaris* eggs are exposed to x-rays generated at 1,000 kv., it is necessary to specify not only the intensity of the x-rays, but also the configuration and composition of all surrounding material from which ionizing electrons can reach the eggs. This is most readily done if the test object is closely surrounded by a layer of tissue-like material at least as thick as the effective range of the electrons. Then the electrons which enter the test object from the surrounding material will just compensate for the loss of electrons from the test object to its surroundings.

Under therapy conditions, the cells receive full electron compensation except at the surface, where, with a beam which is limited by diaphragms, as is always the case with x-rays, there will be a shortage of electrons. It is a question whether the deficit which exists at the depth of the dermal capillaries concerned with erythema production is sufficient to be of practical importance at 1,000 kilovolts. We are not concerned here with the total length of the crooked tracks of the electrons, as revealed in Wilson cloud chamber photographs, but rather with the effective range obtained from experiments on the penetration of electrons through thin plates. According to the data of Varder (18), the fastest forward recoil electrons produced in appreciable amount at a tube voltage of 1,000 kv. can be detected through a thickness of tissue of about two millimeters. However, the fraction of the total incident electron energy which can penetrate to this depth is extremely small (11), and probably is not significant at depths of more than about 0.5 millimeter. Furthermore, the surface deficit is by no means complete, because of electrons contributed by the air and filter in a greater or less amount depending on diaphragming conditions. Even with radium gamma rays, which give some recoil electrons detectable through a centimeter of tissue, Stahel, Simon, and Johner (19) were unable to observe significant differences in the erythemas produced even when foils of different metals were placed

in contact with the skin, although such differences were readily obtained with *Drosophila* eggs, photographic films, and a thin-walled ionization chamber.

Thus it seems unlikely that at 1,000 kv. any very considerable diminution in skin damage will be found to result from electron deficit at the surface. This effect should, of course, not be confused with the effect of back-scattered x-rays on skin dose at different wave lengths. This latter question has been discussed by Lauritsen in some detail (13).

The definition of the "roentgen" is ambiguous with regard to the inclusion of the ionization due to the different types of secondary x-rays generated in the test volume of air. For this reason, and because of the inadequacy of intensity in roentgens as a specification of surface dose, it has been urged that a better experimental basis of dosage should be developed. As yet, however, no substitute physical method is available. Pending the development of such a method we may consider the possibility of measuring intensity in roentgens up to 1,000 kilovolts.

OPEN CHAMBER MEASUREMENTS

The possibility of measuring gamma rays in roentgens by the open chamber method has been investigated by various workers (1, 4, and 14).

The definition of the "roentgen" demands that all of the ionization due to the secondary electrons produced in the test volume of air should be measured. In the open chamber, as applied at ordinary voltages, this is accomplished through a process of compensation whereby the ionizing electrons which are lost from the test volume are replaced by others entering from the outside. With gamma rays, this compensation would require a chamber several meters long. The use of such a chamber with available quantities of radium seems to be out of the question on account of serious technical difficulties connected with diaphragming, current measurement, and disturbing effects of secondary radiations. These same difficulties, in a lesser degree, apply to x-rays produced at voltages above 400 or 500 kilovolts. It may be possible with suitable precautions to make open chamber measurements up to 1,000 kv. with reasonable accuracy, but the question calls for further study. In any case the apparatus must be inconveniently bulky, the distance between the limiting diaphragm and the collector being especially important (1).

The difficulty encountered in using the open chamber with high voltage x-rays and gamma rays has stimulated considerable interest in the concept of an "air-walled" chamber, introduced years ago by Fricke and Glasser. The definition of the "roentgen" demands that all ionization resulting from energy absorbed in material other than air shall be excluded from the measurement. According to the air-walled chamber idea it should be possible to compress the air surrounding the test volume into a solid shell without altering the compensating interchange of secondary electrons between the test volume and its surroundings. If, instead of this imaginary shell of compressed air, we substitute a wall of material having the same atomic properties as air with regard to the absorption of x-rays and secondary electrons, then we would have what is called an air-walled chamber which should measure x-rays directly in roentgens. Encouragement was given to this point of view by some theoretical treatments of the problem, especially that of L. H. Gray (9). Recently a number of authors have made measurements on radium with thimble-type chambers and published their results expressed in roentgens. Other writers, for example Edith Quimby (17), have insisted that it is not proper to express such measurements in roentgens without first re-defining the roentgen.

Considerable weight has been lent to the latter point of view by the large discrepancies which have existed between the results obtained by different investigators for the intensity of the gamma ray output of radium. However, recently published work has somewhat improved this situa-

tion. Some of the more discordant results were obtained with chambers the walls of which were not thick enough to exclude electrons from surrounding objects. Approximate constancy of ionization for wall materials of atomic number up to aluminum has been found by two experimenters (5, 16). On the other hand, Mayneord and L. H. Gray are both reported to have found differences within this range of wall material (8). An outstanding serious discrepancy of 30 per cent between values obtained with thick graphite chambers by Mayneord and Roberts (14) and by Friedrich, Zimmer, and Schulze (6) has been removed by revised values which have just been published by Friedrich and Schulze (5). The average of the recent measurements with thick-walled chambers now agrees closely with the earlier value of Glasser and Mautz (7).

If it could be established that suitably designed thimble chambers can measure gamma rays accurately in roentgens, it probably would follow that such chambers would also measure filtered 1,000 kv. x-rays correctly.

The statement in the last paragraph applies to measurements in air without scatter. On the other hand, in a water phantom, a part of the radiation is degraded, as a result of repeated scattering, to wave lengths for which the photo-electric type of x-ray absorption becomes important even in light elements. The possibility of making correct "air-wall" measurements with such a mixture of wave lengths is much more doubtful than in the case of short wave lengths for which the Compton scattering type of absorption alone is effective. Miehlnickel (15) has obtained results with walls composed of carbon and silicon in different proportions which he interprets as indicating the impossibility of making a thimble chamber which will have wave length independence over the whole x-ray range, and at the same time be "air-walled" in the sense of giving correct absolute values in roentgens. The question obviously calls for further study. In the meantime, data by various workers, Failla (3) and Keller (12), for example, are sufficient to show the importance of even small changes in wall composition on depth measurements.

It is worthy of note that the values of gamma-ray intensity obtained by thimble chambers and other indirect physical methods of measurement average 60 per cent higher than the values obtained from biologic indicators which have been calibrated against standard open chambers for x-ray wave lengths (2). The advantages offered by *Drosophila* eggs as a means of measuring directly the biologic effectiveness of radiation over the whole range of wave lengths used in radiotherapy will be discussed in another paper in this symposium. From a physical standpoint it may be said that for measurements in water or tissue these eggs are nearly ideal, since the whole problem of "air equivalence" of walls ceases to exist. Also, their small size of not over 0.2 mm. diameter is very advantageous in places where the intensity is changing rapidly with position, as in the case of measurements close to a radium source, or at the surface of a water phantom.

As an interesting example of the difficulties which are still being discovered in connection with the indirect physical methods of measuring free air ionization in roentgens for gamma rays, it may be mentioned that Stahel (16) has recently found that his calibration of an ionization chamber by calorimetric measurements of gamma-ray absorption in hexane gives a value for energy in ergs per roentgen over 100 per cent higher than the results obtained by other methods. He ascribed this difference to exothermic chain chemical reactions initiated by the gamma-ray energy and affecting the calorimetric measurements. It would seem possible that in some absorbing materials not only additional heat but also additional ionization might be produced by such secondary chemical processes.

MEASUREMENT OF WAVE LENGTH

Crystal spectrometers have been designed by a number of experimenters,

which permit measurements with voltages up to the neighborhood of a million. These measurements are difficult because of the extremely small deviations suffered by such short wave lengths, and they are entirely unsuitable for routine use outside of a physical laboratory. Most of the observations with high voltages have been correlated with voltage measurements made with large sphere gaps, using the calibration curves of the American Institute of Electrical Engineers. These values have recently been found to be too high by about 7 per cent in the neighborhood of 800 kv. by two independent methods (10). Likewise Tuve, at Washington, found that his sphere gap was indicating 30 per cent too high, presumably due to corona and space charge in the air of the room, thus indicating that sphere gap measurements should be used only with considerable discretion. Lauritsen has found that, contrary to the case with low voltages, a point gap is more dependable than a sphere gap at high voltage. As with low voltages, the values obtained by absorption measurements on the radiation emitted may be used as a measure of quality. Such measurements demand considerable care in the choice of experimental conditions and in the interpretation of the data.

It may be mentioned that the measurement of tube milliamperage, which at low voltages is so useful as a means of maintaining a constant output, encounters complications at high voltages partly in connection with wave form effects and partly as a result of gas discharges in the tube.

SUMMARY

Summarizing, it may be said that the difficulties which are met in making open chamber and "air-wall" chamber measurements up to 1,000 kv. have not yet been completely solved. No physical method at present available can be depended on to measure correctly the mixture of primary and degraded radiation found at a depth either in a water phantom or under therapy conditions in a patient. The ionization produced at the surface of a water phantom by a diaphragmed beam is not uniquely determined by the intensity of the direct and scattered x-rays at the surface because of incomplete compensation of long range electrons. Whether this fact possesses any practical importance with regard to skin erythemas for 1,000 kv. x-rays is doubtful.

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THE BIOLOGICAL ROENTGEN[1]

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MEASUREMENT of the intensity of x- and gamma-rays by means of living organisms and tissues as indicators of dosage has been a common practice for many years. As early as 1915, Ritter correlated the amount of effect of x-rays on growing seedlings with doses measured by the pastilles then in use. Later Jüngling employed both beans and mice for similar measurements. The mice and other large laboratory animals proved unsatisfactory for the purpose because of complications which were not then understood. To simplify the experiment and to obtain clear-cut results, cells and small organisms have been found more useful. In these, scattered radiation can be disregarded; the entire organism is uniformly irradiated, and the complications met with when a small part of a large body is exposed are absent. The variety of biological materials which have been used in these experiments is surprising. Bacteria, yeasts, and spores of various kinds; algæ and seeds of different sorts; protozoa, the eggs of worms, insects, frogs, and salamanders; tadpoles, chick embryos, and larval tissues; water fleas; tissue cultures and tumor particles—all of these have yielded valuable information for the solution of radiological problems.

The reaction which is most often used as a criterion of the effect of radiations involves a fundamental characteristic of living protoplasm, namely, the power of growth and repair. A sufficient dose alters the rate and direction of growth. Cell division is slowed down, with the result that development is stunted or abnormal; or it may be completely stopped by death. Even in adult tissues the effect which is measured is of the same order. Radiations retard the process of regeneration, so that damaged cells cannot be replaced by healthy new growth, and injury ensues. This change in the rate and direction of growth is most easily measured in small, actively growing cells and organisms.

The relation between dose and amount of effect is illustrated by experiments on the eggs of the fruit fly, *Drosophila*. The criterion of effect is the proportion of eggs in a sample which survive and hatch as larvæ. In Figure 1 are shown the results of more than two hundred tests in which various doses, measured in roentgens, were administered under definite experimental conditions. It is clear that the percentage of eggs surviving after each dose is fairly constant. From the curve, drawn to fit the data, one may determine the survival percentages which may be expected to follow any dose within the range shown in the figure. The same procedure is carried out when other kinds of test objects are used. Thus, the ratios between the number of mitoses in irradiated tissue culture preparations and in the controls, or the proportion of bacteria which form colonies after receiving definite doses of radiation can be expressed by a similar graph.

The curve shows that the amount of effect differs greatly among similar individuals. Some are killed or injured by small doses, while others remain alive even after heavy doses. This is because they differ in sensitiveness to radiations, as well as to all other injurious agents. It is also apparent that the results of repeated tests made under exactly corresponding conditions are by no means identical. Differences always occur, but in favorable material they are not great, as the results shown in Figure 1 indicate.

[1] Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, at Detroit, Dec. 2–6, 1935.

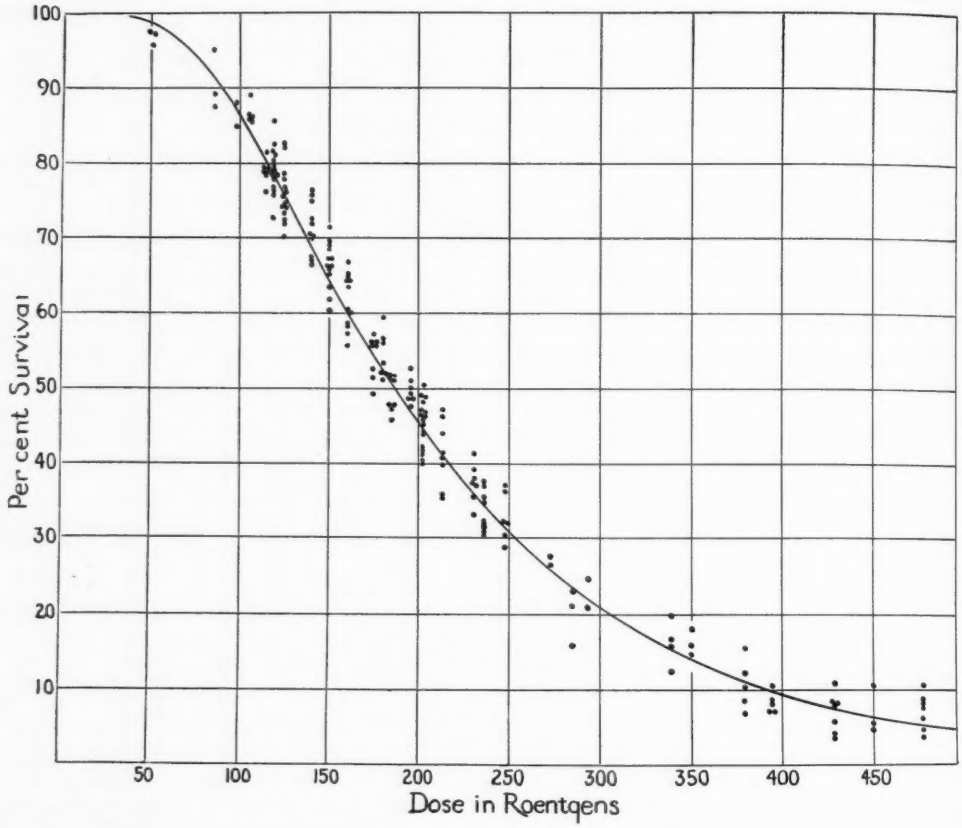

Fig. 1. Graph demonstrating the precision of the *Drosophila* method. The results of 209 tests show the amount of variation which may be expected when the same doses are given to different samples of eggs.

In the tests from which these results were obtained, the potential used was 120 kv., the filtration being 0.25 mm. Cu and 1 mm. Al. Statistical analysis shows that the probable error of a single observation is ±3 per cent. The maximum deviation is 7 per cent. These tests were made over a period of five years, during which time the stocks of wild flies which furnished the eggs were repeatedly changed; but the eggs have maintained the same average sensitiveness. Experiments made by others in this country and in Germany show that eggs from any stock of these wild flies are nearly alike in their response to x-rays (5). In this respect they are superior to the usual dosimeters, which must occasionally be recalibrated.

So constant and dependable is their response that it can be used as a measure of dosage. Thus, if half of the eggs survive after receiving about 190 roentgens, it is also true that when this proportion survives after an exposure to an unmeasured dose, the eggs must have received about 190 roentgens. So, also, if any other percentage of survivors is obtained, the dose which was given can be determined with considerable accuracy by reading from the curve the number of roentgens corresponding to that percentage.

It has been customary, when recording survival percentages obtained in tests with *Drosophila* eggs, to note the dose in roentgens, as measured in this way. The number thus obtained is called the "biological dose," and is expressed in "biological roentgens." Strictly speaking, this use of the term "roentgen" is in-

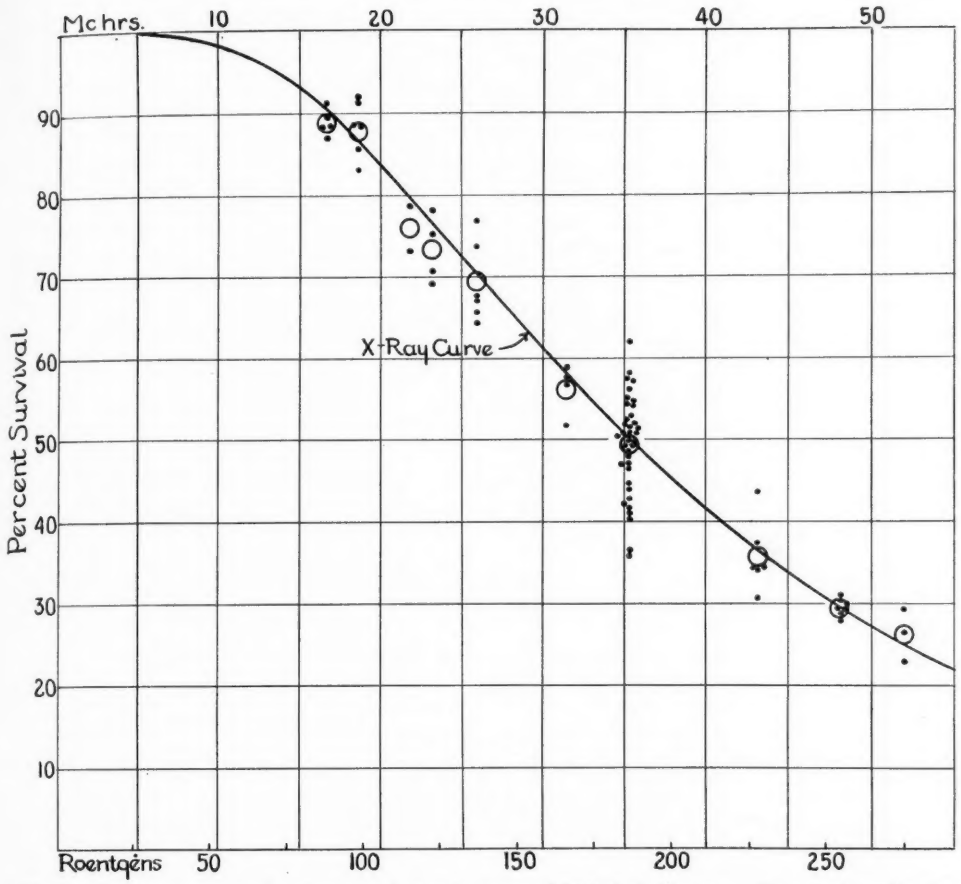

Fig. 2. The measurement of gamma-ray dosage in terms of biological roentgens. By superimposing the gamma-ray survival curve on the x-ray curve, the number of biological roentgens corresponding to one millicurie-hour of gamma radiation (under the conditions specified) can be determined.

correct, but it is a convenient way to compare the magnitudes of the biological and physical doses. Obviously, in the series of experiments recorded in Figure 1 the two units are equivalent; but they are also equivalent over a wide range of wave lengths. Thus, in tests made with Grenz rays produced at 12 kv., the doses determined by the biological method and by the most careful open-chamber methods agreed within 1 per cent (6); and at higher voltages they also agree, as will be shown presently.

But if the two units are equivalent, why should the biological method be used at all, especially since it is time-consuming and requires care and experience in its use? Three experiments illustrate its value. First, it has been used in making depth dose measurements. More than ten years ago, Jüngling (4) and Glocker (2) employed bean seedlings for this purpose. Recently, Hussey has used *Drosophila* larvæ as test objects for determining depth doses in paraffin, and I have employed the eggs of these flies in the measurement of depth doses in a water phantom. It is probable that the biological material responds to soft, scattered radiation which ordinary dosimeters fail to measure accurately. Thus the dose measured in biological roentgens may be greater than that measured by physical means, but the former more

correctly expresses the activity of the radiations at varying depths below the surface.

A second application of the biological method of measurement is in the determination of the relation between wave length and biological effectiveness. The results of early experiments on this subject were contradictory because many times the biological conditions were not good, and because accurate physical measurement was impossible. But as these sources of error have gradually been eliminated, the results have become more and more concordant. Tests with *Drosophila* eggs show that equal doses of wave lengths produced at potentials between 12 and 550 kv. result in equal quantitative data (6). The same conclusion has been reached in tests with protozoa, wheat seeds, peas, beans, the eggs of *Ascaris*, of the green bottle fly, tumor tissue particles, and tissue culture preparations. Evidence from a very different source is presented by Timoféeff-Ressovsky, who shows that the number of mutations produced in *Drosophila* by radiations is independent of wave length, and is purely a function of the dose (7). In such cases, the dose, expressed in biological roentgens, is equal to that expressed in the physical unit.

In the third place, fly eggs or other suitable material can be used to measure the activity of gamma rays. Such an experiment is rendered difficult by the fact that the eggs must usually be exposed at very short distances from the source, and if an extended source, such as a tube or plaque, is employed, the intensity will not be uniform over the field occupied by the test objects. This difficulty has been avoided by Exner and Packard (1), who used an applicator in which highly concentrated radon was held in a bulb so small that it could be considered as a point source. This was enclosed in a spherical shell of Pt 0.5 mm. in thickness, which served as a filter. Outside of the latter was a shell of bakelite, 4 mm. in thickness, the surface of which was everywhere 1 cm. from the source. The eggs were placed on this surface. In such an applicator the standard conditions for the measurement of gamma rays are realized. The eggs were removed after they had received various doses measured in millicurie-hours. When the percentages of survivors were plotted in the usual way, the points were found to lie along the curve already obtained in the x-ray experiments (Fig. 2). The course of this curve, therefore, is not affected by the wave length of the radiations used. It is now possible to determine directly the gamma-ray dose in terms of biological roentgens. For example, 50 per cent of the eggs survive an exposure of 38 millicurie-hours, but this proportion is found also after an exposure to 190 roentgens. The two doses are, therefore, equivalent in their biological effect under the conditions of this experiment. In other words, one millicurie-hour is equivalent to five biological roentgens.

This value is below that found by many physicists, who state that under the same conditions of filtration and distance, one millicurie-hour equals from eight to ten roentgens. The reason for this difference cannot now be stated with assurance, but it is probable that the values determined by physical methods may vary with the geometrical form of the thimble chambers employed, and that they may prove to be much too high. Another point to be considered is that, whereas the thimble chambers record the average intensity in a volume of air two or more millimeters in thickness, the eggs register the intensity at a point, since their diameter is a small fraction of one millimeter. This is important in view of the fact that the intensity of radiation changes very rapidly in the short distances which are used in these experiments.

The experiments with fruit fly eggs and other test objects show that it is possible to measure accurately the activity of x-rays and gamma rays in terms of the biological roentgen; and it is the biological activity of these rays which is the salient point in dosage.

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THE RATE OF RECOVERY OF HUMAN SKIN FROM THE EFFECTS OF HARD OR SOFT ROENTGEN RAYS OR GAMMA RAYS[1]

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IT is well known that a given quantity of radiation is better tolerated by human tissues if it is administered in small doses over a long period of time, than in a single dose or in a few large ones within a short time. The greater the fractionation, the more radiation can be delivered. This is obviously because in the intervals the tissues recover to a certain extent from the damage caused by the radiation. If this recuperation were the same for all tissues, there would be no advantage in dividing the dose; the normal tissues would tolerate more, but so would the diseased tissue. However, it has been found clinically that in many types of malignant tumors it is possible by dividing the doses to produce regression of the lesion without marked permanent damage to the normal tissues, whereas this was usually impossible with a single massive dose. This means that recuperation must proceed more rapidly in the normal than in the diseased tissues in such cases.

In some anatomical areas, the breaking down of the skin is one of the limiting factors to the amount of radiation which can be given. In others, the possibility of lymphedema and late necrosis of the deeper tissues will be the controlling factor in the amount and the method by which it is administered. It is important, however, to know how the skin behaves under different conditions of irradiation.

Since the beginning of divided dose methods, observations have been made on the amount of radiation tolerated by the skin under different schemes of treatment. However, the results obtained by different observers show wide discrepancies. In most of the published reports, the data presented are completely inadequate to support the conclusions drawn, observations having been made on only a very few cases (four or five!). In some instances, results obtained with one set of conditions have been made the basis for conclusions regarding quite different types of radiation or schemes of fractionation. Elaborate methods of treatment have been developed on meager experimental data.

A review of the literature emphasizes the statements just made. It may be well to examine the data which have been most widely accepted.

Kingery (1), having observed that more radiation could be delivered if the dose was divided, realized that this must be due to recovery of some sort. He supposed that irradiation produced some hypothetical decomposition product in the tissues. The rate of loss of radiation effect would be in direct ratio to the elimination of this decomposition product. He assumed that this rate of loss would follow the same law as certain other chemical and biologic reactions, which could be represented by a logarithmic curve. *Note that he assumed a logarithmic curve, and then set about proving its existence.* Working with low voltage unfiltered roentgen rays, he found that a full dose could be repeated after 14 days. He does not specify what he means by a full dose, nor describe the effect produced, nor tell how he decided in favor of 14 days rather than—say—12 or 16. Nor does he specify the number of patients used in making the determination, nor give any idea of how the reactions differed among them. However, he went on to determine that 75 per cent of the full dose could be repeated after seven days, and 50 per cent after three and one-half days. On this basis it is reasonably assumed that the residual effects after three and one-half and seven

[1] Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, at Detroit, Dec. 2–6, 1935.

days are 50 and 25 per cent, respectively. These results apparently verify the original assumption of logarithmic loss of radiation effect. The curve passing through the experimental points can be expressed by an exponential equation of the form:

$$Q = Q_0 e^{-\mu t},$$

where Q_0 is the initial dose of radiation, Q is the amount remaining after the time t, e is the base of natural logarithms, and μ an exponent which depends on the rate of recovery. Since it is known that half the effect is gone in three and one-half days, the equation becomes:

$$50 = 100e^{-3\frac{1}{2}\mu}.$$

This may be solved for μ, which is found to be 0.198. Putting this value for μ in the first equation, the amount left at the end of one day is found to be 82 per cent, which corresponds to a loss of 18 per cent of the effect of the radiation during the first day. It is, therefore, assumed that if 18 per cent of the original dose is added daily, the tissue should be kept at the "*saturation*" point for radiation effect. With the quality of radiation and the type of treatment used, Kingery satisfied himself that this was true clinically. He apparently made no effort to test any other type of curve, any other daily factor, or find the limitations of his method.

Pfahler and Weatherwax (2, 3, and 4) have greatly extended Kingery's method and his conclusions, without, however, having done any actual experimental work. Based upon clinical experience as to when it is possible to repeat a full dose, for various qualities of radiation, values for μ in the above equation have been worked out, and from these the daily loss for the types of radiation in question. Since it is not known what amount of radiation effect may still be present in the tissues when the dose can be safely repeated (say, 1 per cent or 10 per cent), and since the interval is stated in rather wide terms (from 8 to 12 weeks in a given type of radiation), it is evident that the value of μ, and hence of the daily loss of radiation effect, must have a rather wide range. However, a value of 6 per cent per day is accepted for 200 kv. x-rays filtered by 0.5 mm. of copper, and it is assumed that the daily increment of this amount will maintain the tissues at a constant point as regards effective radiation. This hypothesis is based on the assumption that skin recovery must follow a simple exponential law.

This value of 6 per cent recovery in a day is very much less than that which has been found experimentally by any investigator, no matter how small his series of tests. Since, however, this factor is obtained from an entirely different type of observation than those about to be discussed, it is not surprising that they do not agree. This difference will be discussed later in the paper, in relation to the experimental results herein reported.[2]

The experimental data in the literature may be briefly reviewed. With the exception of Kingery's, already mentioned, they refer to radiation of the quality ordinarily used in deep therapy, namely, from 160 to 200 kv., and from 0.5 to 2.0 mm. copper filter. The intensities used by various investigators ranged from 4 to 60 r per minute, but for any single experiment reported, the intensity was kept constant.

Finzi (5) found by clinical tests on many patients that 200 per cent of a mild erythema dose, given in four equal doses spread three or four days apart, produced the same skin reaction as 100 per cent at one sitting.

Stenstrom and Mattick (6) treated two adjacent 10 × 15 cm. areas on the breast in five cases of carcinoma. The upper always received 100 per cent of their erythema dose, and the lower 4 × 30 to 4 × 37.5 per cent, at about three-day intervals. The tabulated observations show wide variations in the results. Their conclusion that the data indicate a recov-

[2] Since the present paper was written, an article has appeared by Pfahler in which he states that, as a result of Reisner's work (herein discussed), he feels that the saturation dosage at any point or any day should be increased by 20 per cent (12).

ery of 8 per cent daily seems quite unjustified, yet this figure is often quoted.

Liechti (7) used a more satisfactory method for making such a comparison. He irradiated on one thigh of each of 13 individuals, three small fields, with 60, 80, and 100 per cent of a sharp erythema dose. On the other thigh he used three separate exposures of 33.3 per cent, at different intervals, from 26 minutes to 96 hours. He found no difference between the single exposure and the divided doses for intervals less than 12 hours. For 24-hour intervals he found 3 × 33.3 per cent equal to 85 per cent at one sitting; for 48-hour intervals to 75 per cent; for 72-hour intervals, to 60 per cent. *However, each of these findings is based on only two patients.* It is to be regretted that he did not complete a larger series of these tests.

Holfelder (8), using small (2 × 2 cm.) fields on each thigh of six individuals, tested various divisions of irradiation based on Pfahler's saturation curves, and came to the conclusion that the recovery factors given were much too low; he did not, however, derive factors of his own.

Borak (9) treated three small series of patients with 180 r daily. Three cases were given 10 × 180 r, and showed nothing; two cases with 12 × 180 r showed strong pigmentation; one each with 15 and 18 × 180 r had marked epidermitis. Since these three groups were treated for different lesions on different parts of the body, no conclusion seems justified from so few cases. If the groups had been larger, worth-while data would have been obtained.

It is apparent that all the reports thus far mentioned are based upon very scanty data; the literature contains others, drawing conclusions from even fewer cases. Since it is known that there are marked differences in the reactions of various individuals to radiation, it should be evident that before any conclusion can be reached it is necessary to make enough tests to obtain an *average* effect. Two such investigations have been published.

Reisner (10) made an extensive study of erythema reactions, using an erythema meter to determine the intensity of the reaction, and following each test by daily observations over a period of several weeks. His standard reaction was a very sharp erythema, produced by 1,000 r (measured in air) on a field 2 × 2 centimeters. Such a reaction is difficult to specify exactly. However, in every test, he plotted the daily observations as a curve, so that comparisons may be made on various bases. He used six small fields on each thigh. One field on every patient was given the standard dose, the others, various combinations, so that direct comparisons could be made. A considerable number of individuals were used, so that the final results represent adequate averages. With equal daily treatments, Reisner found the doses given in Table I to produce the same results.

TABLE I.—VARIOUS FRACTIONAL DOSES WHICH PRODUCE THE SAME EFFECT IN HUMAN SKIN, ACCORDING TO REISNER

No. Irradiations	No. Roentgens per Irradiation	Total Roentgens	Percentage Total Dose
1	1,000	1,000	100
2	650	1,300	130
3	500	1,500	150
4	400	1,600	160
7	300	2,100	210
12	200	2,400	240
27	100	2,700	270

In order to find the shortest interval during which recovery could be shown, he used 2 × 50 per cent on several fields, varying the interval between one and 12 hours. After four hours, the divided dose gave a less marked reaction.

The total dose which gave the standard effect in a given number of days could be given in equal daily doses; in doses twice as great given every second day, or three times as great given every third day, without producing marked differences in the reaction curves, although the final result was usually somewhat less marked with small daily doses.

Duffy, Arneson, and Voke (11), believing that the sharp erythema generally used as the standard reaction could not be deter-

mined as accurately as a threshold effect, and recognizing that many tests must be made in order to obtain average results, carried out an extensive series of tests on this basis. The reactions from two equal doses given at 24- or 48-hour intervals were compared with those from the standard single dose. Their fields were 10 × 10 cm. over the extensor surface of the forearm, their standard threshold dose, 525 r (measured in air). (This field, which seems rather large, was chosen because it was comparable with the fixed field irradiated by the four-gram radium element pack of the Memorial Hospital, since it was planned to compare reactions produced by the two types of radiation.) They found the following doses to give the same final results:

Single irradiation, 525 r = 100 per cent
Two irradiations, 24-hour interval, 2 × 400 r = 150 per cent
Two irradiations, 48-hour interval, 2 × 425 r = 160 per cent.

They conclude that 69 per cent of the effect of the first exposure is lost in 24 hours, or 76 per cent in 48 hours. Their method of arriving at this figure is as follows: Of the first 400 r, enough must remain at the end of 24 hours to give, when added to the second 400 r, effectively 525 r; that is, 125 effective r[3] must be left. This implies that recovery from the effect of 400 r − 125 r or 275 r has taken place. Expressed numerically, recuperation equivalent to $\frac{275}{400}$ or 69 per cent has occurred.

The same calculations applied to Reisner's data give 46 per cent in 24 hours. These two results are not in good agreement, but both are considerably higher than the "saturation" values. Since Reisner's observations were made on a very sharp erythema, and Duffy, Arneson, and Voke's on a threshold, it is not surprising that the results do not agree. It might be expected that there would be greater recovery in the case of the smaller original dose.

The method of Duffy *et al.* seems to offer the best means for obtaining accurate information, even though it be granted that, in general, therapeutic irradiations produce sharper reactions. It was felt desirable to extend their work to other divisions of irradiation and to other qualities of radiation. This has been done, and the results are here presented.

The hard x-rays used were exactly the same as those of Duffy and his co-workers: 200 kv. (peak), 0.5 mm. copper filter, 50 cm. target-skin distance, about 60 r per minute. All doses stated are measured in air. The fields used were 10 × 10 cm. over the extensor surface of the forearm of male patients, mostly from the intra-oral clinics of the hospital. Since the present authors had assisted in reading many of the erythemas in the earlier work, and expected that Dr. Duffy and Dr. Arneson would read some of the later ones, it was felt that the results of both series would be consistent, and that finally all the data could be handled together.

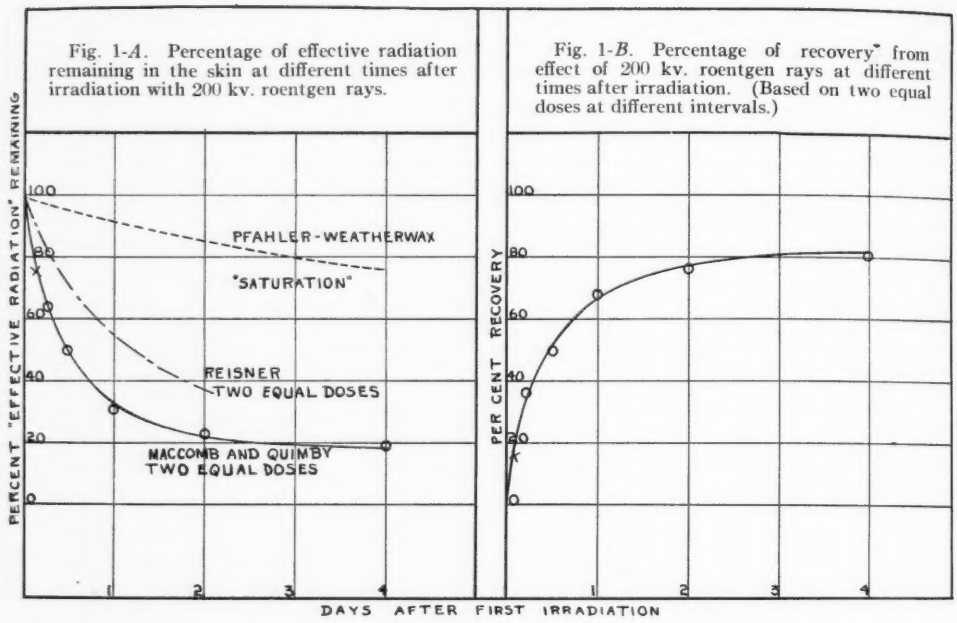
The threshold skin dose[4] for all x-ray tests is defined as that quantity of radiation which, delivered in one exposure, at the rate of from 40 to 60 r per minute, produces in 80 per cent of all patients a visible pigmentation within one month, and in the others no visible reaction. For gamma rays, the intensity of irradiation is much lower, and the time limit must be extended to six weeks, but the method of applying the test is the same.

[3] The term "effective r" must not be interpreted to mean that any number of roentgens of radiation actually remain in the tissues. The above calculations do not in any sense imply a decay of radiation analogous to the decay of radon. At present there is no information regarding the mechanism of the action of radiation on tissues which is applicable to this problem. It can only be said that the radiation acts *as if* there were a certain amount remaining at any specified time.

[4] In former papers, this quantity of radiation has been referred to as the *threshold erythema dose*. This has given rise to some misunderstanding in other institutions, where different criteria of *erythema* are used. Since what is observed is not actually an erythema, which may be transient, but a pigmentation which persists for some time, it seems better to refer to this dose as the threshold pigmentation dose, or simply the threshold skin dose.

Fig. 1-*A*. Percentage of effective radiation remaining in the skin at different times after irradiation with 200 kv. roentgen rays.

Fig. 1-*B*. Percentage of recovery from effect of 200 kv. roentgen rays at different times after irradiation. (Based on two equal doses at different intervals.)



The paper of Duffy *et al.* presented results for 24- and 48-hour intervals. Longer and shorter ones have now been used, and the final results of the whole series are given in Table II. It is evident from this table that recovery sets in promptly, and at a rapid rate, half of the effect being lost in the first 12 hours. The recovery rate continually decreases, however, so that during the third and fourth days there is only 6 per cent more recovery than during the first two days.

It is of interest to plot these data on a curve to show the variation of loss of radiation effect with time after the first irradiation. This is done in the lowest curve of Figure 1-*A*. Each point on this curve represents the percentage of radiation remaining effective at the time indicated after its administration, as determined in the manner just described, the values being those of Column VII, Table II. They apply only to the case in which the radiation is administered in two equal doses, and when the individual doses are less than the standard threshold dose. The upper curve is based on the Pfahler-Weatherwax saturation scheme, with a recuperation of 6 per cent daily for this type of radiation; the intermediate one is Reisner's, for 24- and 48-hour intervals. The two experimentally determined curves do not differ greatly, in comparison to the divergence of either from the Pfahler-Weatherwax curve. As has already been stated, the experimental ones are for different effects, and are obtained by different methods of observation.

The percentage of radiation effect lost during any period (or the percentage of tissue recovery) is obtained by subtracting from 100 per cent the values of the percentage remaining effective. These values for recovery are given in Column VI, and in the curve of Figure 1-*B*.

It is impossible to express the experimental data by a simple exponential curve. However, any curve may be expressed as the sum of exponential terms, in an equation of the type

$$Q = Q_0(ae^{-\mu_1 t} + be^{-\mu_2 t} + ce^{-\mu_3 t} \ldots)$$

In this manner, curve (1) can be fairly well expressed by the equation

$$Q = Q_0(0.66e^{-1.6\,t} - 0.17e^{-0.52\,t} + 0.37e^{-0.14\,t}).$$

TABLE II.—RECUPERATION OF HUMAN SKIN AT DIFFERENT INTERVALS AFTER ROENTGEN IRRADIATION

I Interval Hours	II Total No. Irrad.	III r per Irrad.	IV Total r	V Total Dose in Percentage of Stand. Single Dose	VI Percentage Recovery during Interval	VII Percentage Remaining after Interval	VIII No.[5] Tests
..	(1	525	525	100)[6]	...	..	65
6	2	320	640	122	36	64	16
12	2	350	700	133	50	50	27
(24	2	400	800	152	69	31	65)
(48	2	425	850	162	76	24	52)
96	2	440	880	168	81	19	8
24	3	275	825	157	(Compare 48 hours, 162 per cent)		18
24	5	185	925	176	(Compare 96 hours, 168 per cent)		6

[5] This column indicates the total number of tests made to determine the tabulated data. It includes, of course, those which were too high or too low, as well as those which finally proved to be correct. Fewer tests were necessary in the present series because the very well established points of the first series made possible close approximations to the correct doses before the experiments were begun. Each point established makes subsequent ones easier.

[6] The value in parentheses are those determined by Duffy, Arneson, and Voke.

However, such an expression is of little value, for it is probable that experimental values for a larger number of days would not fall on the prolongation of the curve.[7]

There is no reason for thinking that the loss of radiation effect should follow a simple exponential curve. Kingery assumed a simple reaction product which he thought should follow a chemical law of mass action. But the action of radiation in producing tissue changes is obviously a complicated chain of chemical and biologic phenomena, and must be much better understood before there is any hope of reducing it to a mathematical formula.[8]

[7] The method of determining the coefficients and exponents in such an expression is too complicated to go into here. It is, however, based upon procedures which render extrapolation beyond the known points of little value.

[8] Since the present article has been written, an interesting theoretical discussion of a variable recovery factor by Hoffman and Reinhard has appeared (14). Using statistical methods, and considering an idealized slice of tissue, they develop expressions for the number of cells remaining undamaged, and for those recovering from damage, under various conditions of irradiation. For certain specified recovery factors for the first 24 hours, including those of Stenstrom and Mattick (6) and of Duffy, Arneson, and Voke (11), they give sets of curves showing possible courses of recovery with different variations of this factor from day to day. So far they have considered only the two cases in which the recovery factor varies linearly and exponentially. From the experimental work herein presented, it appears that, for human skin, neither of these is correct. The authors indicate that they expect to extend their treatment.

A complete dose of radiation is seldom given in two treatments; several are usually administered, at daily or longer intervals. In the lower part of Table II are shown the summations of daily dose to produce the same effect as a single full dose, in three or five daily irradiations.

For convenience in discussion, the various schemes of irradiation which lead to the same final result may be summarized as in Table III. It is interesting to observe that, according to these results, it makes very little difference into how many fractions the total dose is divided, so long as the total time remains the same. That is, 2 × 425 r or 850 r, with a single 48-hour interval, and 2 × 275 r, or 825 r, with two

TABLE III.—RADIATION SCHEMES PRODUCING SAME FINAL RESULT IN SKIN

Roentgens per Treatment					Total	
Monday	Tuesday	Wednesday	Thursday	Friday	Roentgens	Per Cent
525					525	100
400	400				800	152
425		425			850	162
275	275	275			825	157
440				440	880	168
185	185	185	185	185	925	176

24-hour intervals, produced the same final result. This is also true for 2 × 440, or 880 r (96-hour interval) and 5 × 185 r (four 24-hour intervals). In each of these pairs the difference between the two total doses is less than 5 per cent, which, as a

matter of fact, is in closer agreement than can be expected from this type of experimental work.

Reisner found in similar experiments, in which the total time and total dose were larger, that he sometimes produced a more marked effect when he gave fewer stronger individual treatments. However, he shows curves for 4 × 60 per cent in 12 days (1, 3, 7, 12 days) and for 12 × 20 per cent in 12 days (daily), in which, after the thirtieth day the reactions follow the same course up to the fiftieth day, when observations were discontinued. Obviously they could not run parallel during the first two weeks of irradiation, but the final result is apparently the same.

Some radiologists insist that treatments must be given daily, or even twice daily. Yet if the good result obtained with daily irradiations can be duplicated by using treatments twice as large, given only every other day, the advantages to the patient and to the busy roentgen-ray department are obvious. Of course, the individual treatments must each be less than the threshold dose. The present experiment gives no information as to the recovery when the first dose is itself large enough to produce a visible reaction. Also there is as yet no information available as to the *relative recuperation of the skin and tumor tissue* under the various conditions, and it is only when this is known that one scheme can be definitely stated to be preferable.

The advocates of small daily doses often insist also on low intensity of radiation. In this connection another point may be brought out. From the curve of Figure 1 it would appear that in three hours, 25 per cent of the effect would be lost, 75 per cent remaining. (This point is indicated by a cross on the curve.) This shows that two treatments of 300 r each, separated by three hours, would produce the standard effect. This was not tested. However, in the course of another investigation, Dr. Arneson and one of the present authors showed that, when the rate of administration of radiation, of the quality under consideration, was reduced from 60 r per minute to 3.3 r per minute, the dose required to produce the threshold effect was increased from 525 r to 600 r (13). This required just three hours to administer. Therefore, it appears that, as far as the skin is concerned, *and for these short time intervals*, continuous irradiation produces the same result as the intermittent administration of two equal treatments, one at the beginning and the other at the end of the period, if the total dose is the same. This point should be investigated further, for it is of significance with regard to the question of the advisability of the use of high or low intensity in therapy. It suggests that the advocates of protracted, low intensity irradiation might obtain the same result by using high intensity doses at the beginning and the end of their customary irradiation periods.

It might be thought that the curve of Figure 1 could be used to calculate the residual amount from daily treatments for any time within its range. If 5 × 185 r produce the same end-result as 525 r at one sitting, then the sum of the residuals on the fifth day from the five treatments ought to equal 525. That is, when the fifth irradiation is given, there should be left 32 per cent of the radiation administered the day before (one day recovery), 24 per cent of that given two days before, etc. When these values are tabulated, however, it is seen that this is not the case (Table IV). There is a discrepancy of 30 per cent, which is too much to be accounted for by experimental error.

TABLE IV.—RECOVERY FROM SUCCESSIVE TREATMENTS, CALCULATED FROM CURVE

No. Treatment	Time Elapsed Days	Per Cent Remaining (Curve)	Equivalent r (Per Cent × 185)
1	4	19	35
2	3	21	39
3	2	24	44
4	1	32	59
5	0	100	185
	Total		362
	Threshold Dose		525
	Percentage of Discrepancy		30

It is evident that when daily treatments are given, recovery does not proceed as rapidly as indicated by this curve, which is based on the effect of only two treatments. One obvious explanation suggests itself. The values for various intervals in curve (1) refer to recuperation in previously unirradiated tissue. But when daily treatments are given, only the first is into tissue of that sort, for all subsequent ones the tissue has already undergone a certain amount of damage, and recovery would be expected to be less. Therefore, the only applicable factor in the above table is the one for the first treatment; all the others should be higher.

For special cases these higher factors can be obtained. The method of doing this can best be explained by reference to Figure 2. Consider first the dotted line starting at point A, or 400 r; this point represents the first dose of the amount necessary to produce the threshold effect when given in two portions with a 24-hour interval. It has been shown (see Table II or Fig. 1), that 31 per cent of this is effective 24 hours later. This is indicated at point B, 125 r, or 31 per cent of 400 r. The addition of 400 r to this brings the curve to point C, the 525 r effective total.

It has been shown that three daily doses of 275 r each produce the same result. The solid line, starting at D (275 r), follows the course of this treatment.

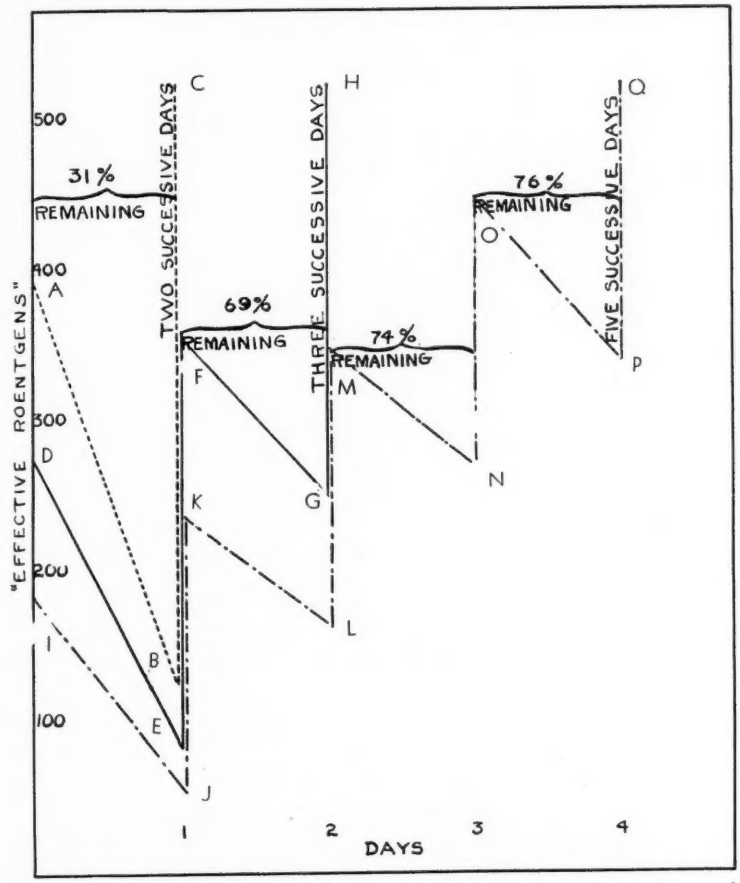


Fig. 2. Accumulation of effect of 200 kv. roentgen rays under various schemes of equal daily fractions. (MacComb and Quimby.)

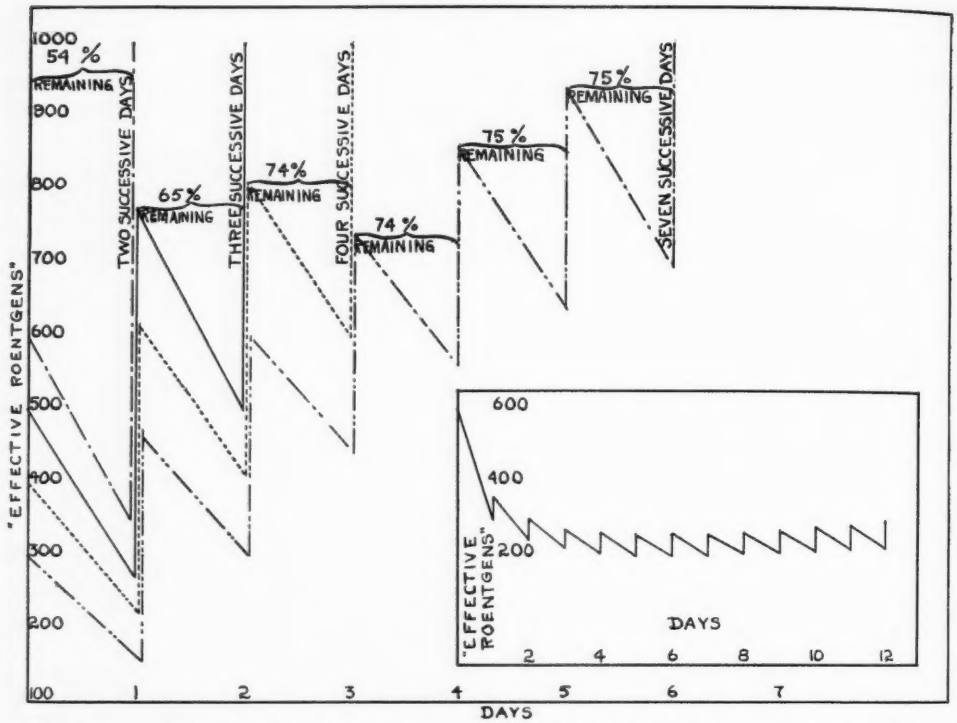


Fig. 3. Accumulation of effect of 200 kv. roentgen rays under various schemes of equal daily fractions. (According to Reisner.) Inset: Application of these factors to saturation technic; 600 r initial irradiation, plus 60 r daily.

After 24 hours, 31 per cent of 275 r, or 85 r effective remain, indicated at point *E*. The second application of 275 r brings the curve to point *F*, 363 r. At the end of the second 24 hours it is not known as yet what part of this will remain, but it is known that another 275 r added to the remainder will produce an effective 525 r. This remainder, then, must be 525 r − 275 r = 250 r. That is, 250 r effective must be left from the 363 r, at the end of the second 24 hours. This is indicated by point *G*. Expressed in percentage remaining, it is $\frac{250}{363}$, or 69 per cent. To this 250 r effective, the third 275 r is added, bringing the total to 525 r. From this experiment it follows that, although 31 per cent of the effect remains after 24 hours in previously unirradiated tissue, 69 per cent remains after 24 hours when it is a second daily treatment.

The process may be carried on, by means of the five-day data, to find the amount remaining for every day up to the fifth. It is not necessary to trace it here step by step; the results are shown in the dashed curve *IJKLMNOPQR* (Fig. 2). It appears that after two treatments the daily recovery does not change so rapidly; in fact, for the last two it is practically the same, 75 per cent effectively remaining, or the recovery being 25 per cent.

The present experiment offers no means of going further, but Reisner gives data for 7, 12, and 27 daily irradiations. The results of treating his data up to seven fractions in the same manner as the above give the curves of Figure 3. It is of great interest to note that, although his first-day recuperation is less than that found by Duffy and his co-workers, all subsequent ones agree with the values of Figure 2. In this connection it should be noted that,

for the irradiation in two treatments, Reisner's individual doses were greater than the single threshold dose of the present authors. When such a large initial irradiation is given, it should not be expected that recovery would be as great as for smaller ones. For all other fractions, Reisner's doses fall below the threshold dose, and in these cases, values obtained from his data agree with those of the present work. This is significant, for it shows that, even when the final reaction is a very sharp erythema, the recovery factors based on the threshold effect are applicable.

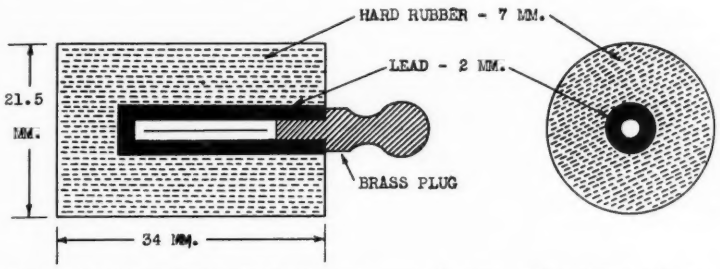


Fig. 4. Applicator for determining gamma-ray skin doses. The radon tube is kept at the center of the space by rolling paper tightly around it.

It would obviously not be expected that 25 per cent recovery would go on indefinitely. There is certainly a point in tissue damage from which there is no recuperation. This point must be approached gradually. When Reisner's data for 12 daily doses are treated as above, it is found that by the eleventh day there is only 15 per cent recovery. By means of his 27-day treatment, it is calculated that after three weeks, daily recovery is less than 10 per cent.

It is interesting in the light of this information to return to the "saturation" technic. Here ordinarily an initial dose, approximately equal to, or only slightly less than, the threshold dose, is followed by small daily increments. From Reisner's data it appears that recuperation from the initial dose should be of the order of 50 per cent, instead of the 6 per cent postulated by the users of this technic. Successive doses would be recovered from less and less, until after a considerable number of treatments the 6 per cent figure would be approximately correct and "saturation" would be maintained. But it would be a saturation at a level of about half the threshold dose, or less, instead of being just below the full dose. A curve representing this type of treatment is shown in the inset in Figure 3.

No data are at present available for other intervals between irradiations.

With respect to other qualities of radiation, experiments have been commenced with soft roentgen rays and gamma rays.

The soft roentgen rays were generated at 100 kv. peak, at about 50 r per minute, filtered by 1 mm. of aluminium, the target-skin distance being 25 centimeters. The same set-up for size and position of field was used as with the 200 kv. radiation. By a total of 60 tests, the threshold dose for this type of radiation was established as 185 r, measured in air.[9] After 32 additional tests, it was found that the administration of 150 r on each of two successive days produced the same reaction. This implies a recovery of 77 per cent in 24 hours, a figure somewhat greater than for 200 kv. radiation.

For gamma rays, tests were made with the small applicator shown in Figure 4, strapped to the skin in the same region as that used for the other experiments. A total of 36 tests fixed the single exposure

[9] This value should not be quoted in any study of quality effect of radiation. Large fields were used, so that back-scatter plays an important part. For the present study this is immaterial, since the question under investigation is recuperation for a particular type of radiation.

for the threshold effect at 225 millicurie-hours, when the exposure time was between one and three hours. Twenty-eight additional tests established 2 × 160 millicurie-hours as the corresponding dose for the 24-hour interval. This implies a recovery of 60 per cent, which is definitely less than for 200 kv. roentgen rays.

In considering these other qualities of radiation, attention should be called to the varying periods during which it was necessary to follow the tests. The results of the low voltage roentgen-ray exposures could be determined within two weeks. The threshold pigmentation was first obtained after more than two weeks in only three of the 92 tests with radiation of this quality. The corresponding period for 200 kv. roentgen rays is three weeks, only nine of the 257 tests becoming positive after this interval. With gamma rays, pigmentation may not appear until six weeks after exposure. In 10 of the 64 tests this was found to be the case, while in only 17 did it appear within two weeks. This points to some actual difference in the effects produced by the different types of radiation.

For the two types of roentgen rays, conditions of irradiation were practically the same as regards size of field and rate of administration. For gamma rays, both of these factors were different. The irradiated area was not sharply defined, but since the source was a tube 15 mm. in length, placed 11 mm. from the skin, the field was small. Also because of the short distance, the distribution of radiation in the thickness of tissue which is probably involved in the production of skin reaction was quite different from that for roentgen rays. The intensity was such that the time necessary for the production of the threshold effect was about fifteen times as great for gamma rays as for roentgen rays. All these factors may contribute toward making the gamma-ray effect different from that of roentgen rays, resulting in a different recovery factor. However, the fact remains that, for this type of radiation effect, the factor *is* different.

SUMMARY AND CONCLUSIONS

A review of the data available in the literature on tissue recuperation after roentgen irradiation shows that very little systematic study of the problem has been made. Only two reports of detailed investigation were found, those of Reisner (10) and of Duffy, Arneson, and Voke (11). The work of the latter group, on the production of the threshold skin reaction by divided doses, seems to offer the most promising method for further research.

Following their technic, the amount of 200 kv. roentgen radiation necessary to produce the threshold effect, when given in two equal doses, at intervals of from 6 to 96 hours, has been found, also the amount for three daily and five daily doses.

From these data have been calculated the recuperation from the first dose after any of the above intervals. Recovery is found to set in promptly, for even after six hours, 36 per cent of the effect has been lost, and after twelve hours, 50 per cent. It proceeds more and more slowly with longer intervals.

When more than two daily treatments are given, the above values can be applied only to the first; subsequent ones are recovered from more slowly. Values for these subsequent days are calculated and it is found that after the second day the change in recovery rate becomes less. From that time on, recovery proceeds at the rate of about 25 per cent daily to the fifth day, beyond which the data do not go.

Calculations made from the only other extensive data available, that of Reisner, confirm this value of about 25 per cent up to seven days, in spite of the fact that he used a much sharper reaction (1,000 r in air on a 2 × 2 cm. field, instead of 525 r on one of 10 × 10 cm.). This is particularly significant because it indicates that, even when the final result is a very sharp reaction, such as is obtained in clinical practice, recovery factors based on the threshold effect are applicable. For greater fractionation, with correspondingly greater protraction of the irradiation, the daily

recuperation becomes even less. For daily treatments up to 12 days (20 per cent of the standard dose daily), the residual effect progresses slowly up to about 85 per cent, and for 27 days up to about 95 per cent.

For soft roentgen rays and for gamma rays, the factor for the 24-hour recovery has been found, when radiation is administered in two equal doses. For the soft roentgen rays, recuperation is greater than for hard; for gamma rays, it is definitely less.

All the experimental results are consistent with clinical findings; no available clinical data are precise enough to permit the determination of numerical factors.

The authors wish to thank Dr. Duffy and Dr. Arneson for their co-operation in this work. They are particularly indebted to Dr. Arneson for his assistance in making many of the gamma-ray tests. They also wish to express their appreciation to Dr. Failla for his interest and suggestions during the course of the work.

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FURTHER DEVELOPMENT IN SUPERVOLTAGE THERAPY APPARATUS[1]

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THIS paper is the continuation, and, to some extent, an enlargement, of a similar one presented elsewhere (7) on the same subject about two years ago. It deals in the first instance with the latest development of supervoltage roentgen therapy apparatus, but also considers briefly certain other medical possibilities of extremely high voltages. Whereas it may be said that the general principles of engineering design in the high voltage field have been laid down in a most satisfactory way from the beginning, during the past two years numerous technical detail developments have been added which make a review of the entire question of construction worth while.

(A) SUPERVOLTAGE TECHNIC FOR THE PRODUCTION OF VERY HARD ROENTGEN RAYS (ACCELERATION OF ELECTRONS)

(*a*) *Emitting Source (Tube Design)*

(*1*) *Sealed Vacuum Tubes.*—The development of sealed vacuum tubes for increasingly higher voltages has long formed a most intriguing problem of engineering research. From the point of view of therapeutic application, such a tube in appearance represents great simplicity of operation and hence is a most desirable instrument to the practical roentgenologist. However, the three following fundamental difficulties continue to place an upper limit to the engineering skill and ingenuity: the control of the cold cathode discharges, the screening off of the back diffusion electrons, and the assurance of a high vacuum. Through solution, in part or entirely, of some of these difficulties, the upper range of the sealed vacuum tube has been raised during the last year to 400 kv. constant (20 ma.), and Gross (6) a few months ago made public the characteristics of such a tube in a very comprehensive manner. An ever-increasing number of installations is now making good use of this tube (Fig. 1).

(*2*) *Tubes Operating with a Continuous Pump.*—The above difficulties incited research also in another direction. It was thought that, by connecting the roentgen tube to a continuously evacuating pump, a sufficiently high vacuum could be obtained to insure satisfactory operation at increasingly higher voltages. In the beginning, mercury diffusion pumps were used but it was soon found that a liquid air trap had to be placed in the vacuum line between the last stage of the pump and the roentgen tube to remove the condensable mercury vapors collecting at normal temperature. This, then, although the pumping system was quite fast and efficient from the point of view of vacuum production, especially at higher voltages, had the drawback that a large amount of liquid air was consumed, entailing a great expense and considerable care to operate. In 1929, Burch (4) discovered that the method of evaporative distillation can be applied to some derivatives of petroleum, and that from these certain oils can be produced which have exceedingly low vapor pressure at atmospheric temperature. By using such apiezon oils in place of mercury in condensation pumps, a perfect vacuum was obtained without the introduction of a liquid air trap for the cooling of the vapor in the line. This represented a very great advantage, and Allibone and Bancroft (1) immediately undertook further experiments to apply the apiezon oil diffusion pump for the exhaustion of high voltage roentgen tubes.

[1] Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, at Detroit, Dec. 2–6, 1935.

After a few changes, aiming especially to eliminate cracking of the oil, a diffusion pump has been developed which worked so satisfactorily that its use was proposed in preference to sealing of the tube, and, in 1934, Allibone and Bancroft were able to publish their results for the construction of continuously evacuated roentgen tubes (1) up to 250 kv. D. C. (Fig. 2), and Allibone, Beetlestone, and Innes for continuously evacuated thermionic rectifiers (2) up to 300 kv. D. C. (Fig. 5). The introduction of the apiezon oil pump represents a still greater advantage in the range above 400 kv., in that it permits a great simplification of operation with a considerable reduction in cost and an increased efficiency as compared to the old mercury diffusion pump.

The underlying principles of the supervoltage roentgen tubes operating on a continuous pump have been described in detail in our previous paper, and therefore it appears superfluous to give a repetition of the same subject here. Suffice it to say that in the main they are unisectional (Fig. 3) or multisectional (Fig. 4), glass walled or porcelain walled, anode-grounded or mid-grounded, constructed mostly for from 500 to 700 kv. (equiv.), and that a few actually run in the neighborhood of 1,000 kv. The changes which were made in these tubes more recently involve factors of lesser importance, mostly representing problems of technical detail. Mention may be made, however, of two types of tubes which incorporate rather unique arrangements. The first, the tube of Newell, Duveneck, and Hackney (8) is designed to operate on a continuous pump in the range of 400 kv. This tube is unisectional, porcelain walled, and anode-grounded similar to the Lauritsen type of tube, but has two cathode filaments which are mounted 15 cm. away from the target

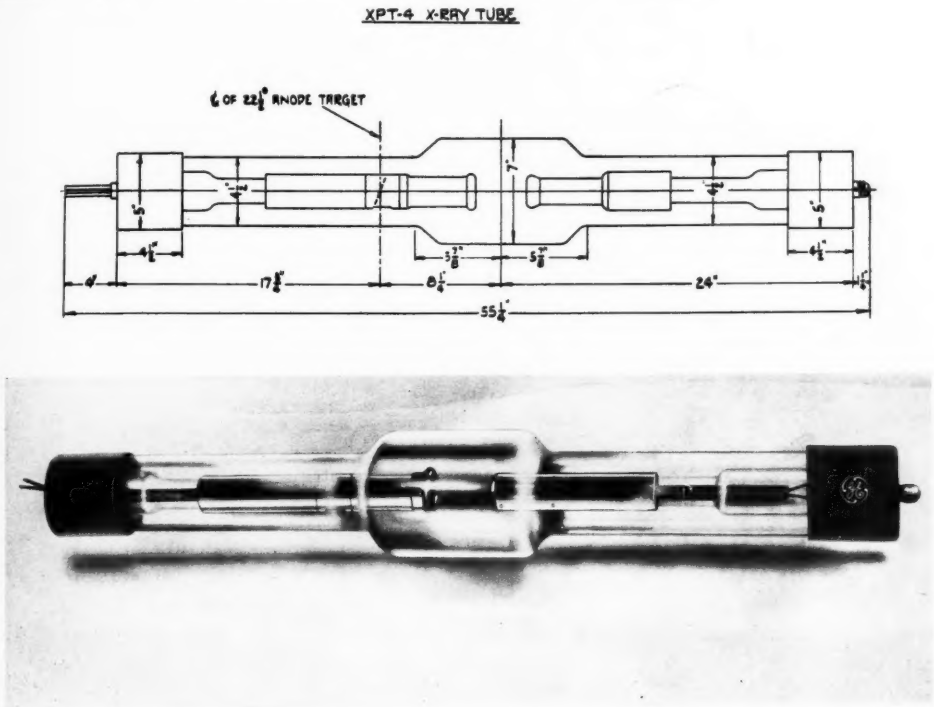

Fig. 1. Sealed vacuum roentgen tube for 400 kv. constant (20 ma.). Above is a diagram of the tube; below is a photograph of the tube. (Courtesy of General Electric X-ray Corporation.)

at the end of a long steel pipe extending axially throughout the entire length of the tube. The target (water-cooled) is roof-shaped with two 45° gold surfaces, potential which must be insulated between the two ends of the tube. The base of the porcelain assembly is supported by a stainless steel cylinder which projects

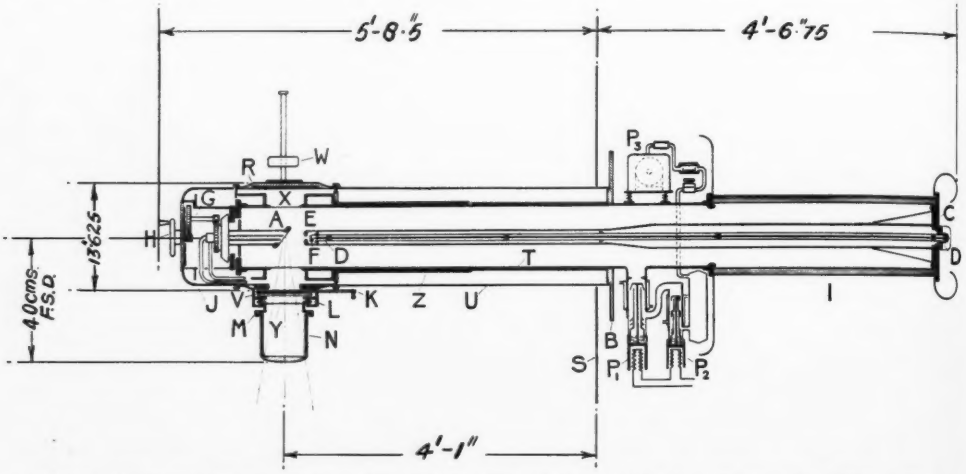

Fig. 2. Continuously evacuated roentgen tube for 250 kv. D.C. (Courtesy Metropolitan-Vickers Electrical Company, Ltd.)

permitting the use of the rays in various directions. Another feature is the fact that a valve is built into the tube itself, to make possible the use of a Villard potential doubling arrangement. The filament of the valve is set, at ground potential, into the brass cylinder of the anode end, just behind the wall, through which the cylinder projects into the treatment room, and the plate of the valve is represented by the cathode pipe. The second is the tube designed to operate with the direct current electrostatic generator of Van de Graaff in the range of 1,000,000 volts, 3 ma. (Fig. 6). Through the courtesy of Dr. Richard Dresser of the Collis P. Huntington Memorial Hospital we are able to give the following description, furnished through the kindness of Mr. John G. Trump of the Massachusetts Institute of Technology: The tube is of the cascade type made up of 15 porcelain sections, about 10 inches in diameter, and provided with diaphragms between sections, which serve to focus the electron stream in its passage from the upper end of the tube to the target, and also to break up the total through the floor of the generator room into the treatment room, the whole arrangement being continuously evacuated by a high speed vacuum pumping system. The filament assembly is located on the upper end of the porcelain column, and will be provided with a total of 8 filaments so that replacement of the filaments will be necessitated only after eight of them successively have been burned out. A demountable water-cooled target at ground potential is attached to the bottom of the stainless steel cylinder. Both cylinder and target are surrounded by a suitable thickness of lead, and ports are provided on two sides and below the target, thereby permitting the treatment of three patients at one time, if desired.

(*b*) *Energizing Source (Generating Plant Construction)*

(*1*) *Induction Coil.*—The use of this type of energizing source, which served as good a purpose in experimental pioneering for the introduction of supervoltage roentgen therapy as the old mercury interrupted Ruhmkorff coil served in the era of the

beginning of roentgenology as a whole, has now, at least for the time being, been discontinued.

(2) *Transformer Circuits.*—The most commonly used circuits in the construction of high voltage generators are those of Latour or Greinacher, leading to direct current constant potential, of Villard, producing a pulsating potential current of Wittka, giving rise, likewise, to a pulsating potential current but with some flattening of the pulsation as compared to the Villard circuit and, finally, the straight alternating current whereby the tube is self-rectifying. Any of these circuits may be used in the supervoltage field in the form of cascaded systems or other suitable arrangements for the excitation of sealed vacuum roentgen tubes as well as continuously evacuated tubes operating with a pump.

An interesting and more recent development is the introduction of continuously evacuated thermionic rectifiers in the circuits (Fig. 5). By doing this one may make use of the half-wave circuit, or the rectifier may be applied advantageously to some of the fullwave circuits, making possible the construction of larger individual units which are then cascaded. In the half-wave circuits, the stray capacities between the rectifiers may be equalized in several ways, the Cockcroft (2) method, lending itself quite advantageously to the association with the continuously evacuated thermionic rectifiers. Through the courtesy of Dr. Finzi and Mr. Allibone, we are informed that a high voltage plant is under construction at Saint Bartholomew's Hospital, London, which will operate in the neighborhood of 1,000,000 volts, and which will make use of two 800,000

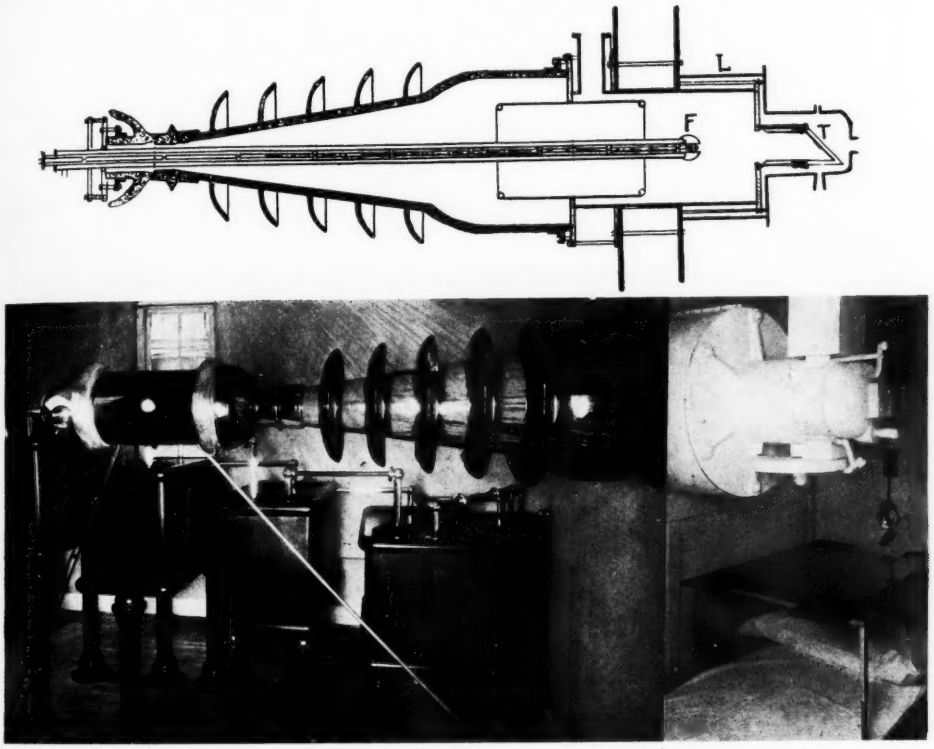

Fig. 3. Unisectional porcelain-walled anode-grounded roentgen tube for 700 kv. constant running on a continuous pump. (Courtesy Kelley-Koett Manufacturing Company.)

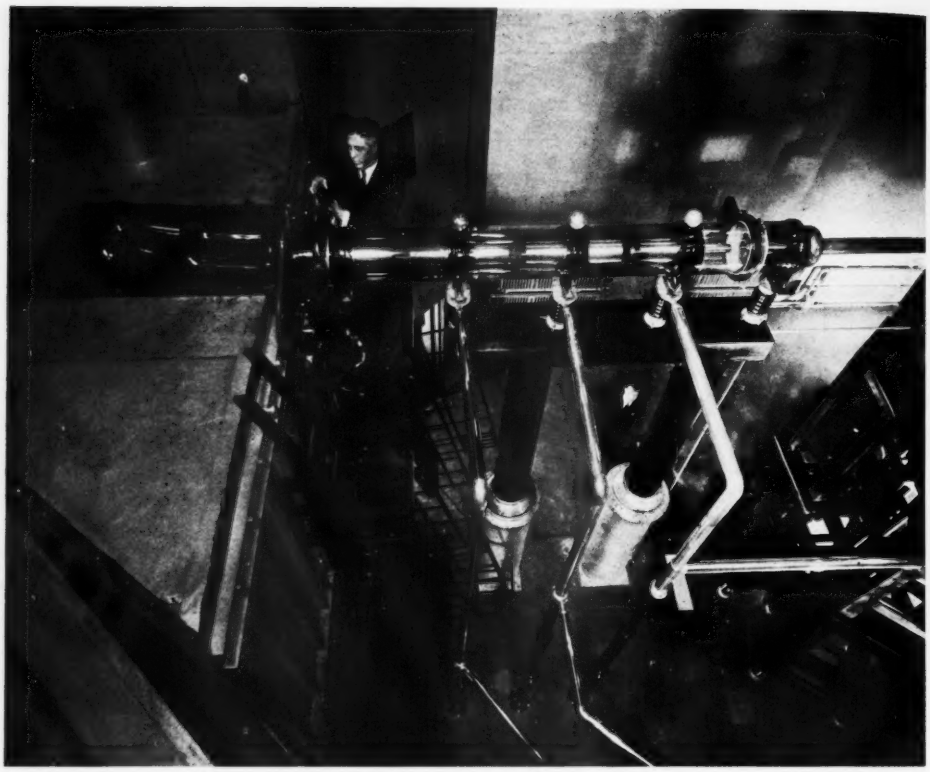

Fig. 4. Multisectional, glass-walled anode-grounded roentgen tube for 900 kv. pulsating, running on a continuous pump. (Courtesy of General Electric X-ray Corporation.)

volt generators designed on the basis of the above principle (Fig. 6).

(*3*) *Static Machine.*—It is the merit of Van de Graaff (13) and his co-workers of having made possible the use of this type of generator for extremely high voltages. The machine which serves a good purpose in the field of nuclear physics (12) is now also being installed for medical use. Thus the high voltage group of the Massachusetts Institute of Technology is designing an apparatus for the Collis P. Huntington Memorial Hospital, aimed to operate at 1,000,000 volts and 3 milliamperes. Again, through the courtesy of Dr. Richard Dresser and the active co-operation of Mr. John G. Trump, we are able to give the following brief description of this apparatus (Fig. 6): The source of high potential is a direct current electrostatic generator of the belt type, which is equipped with current and voltage control so that the potential can be regulated over the full range from about 100,000 to 1,000,000 volts, the fluctuation being less than 2 per cent. The generator has six belts, each three feet wide and travelling with a speed of 5,000 feet per minute, which pass between the grounded base and the high voltage body. The ascending runs of the belts carry negative electricity to the high voltage body and the runs remove positive electricity from the high voltage body. The generator room is rectangular, having inside dimensions of 25 ft. × 23 ft. × 20 ft. 6 inches. The walls and ceiling will be covered by a thin sheet of galvanized metal, so as to limit the influence of the high voltage body to the generator room itself.

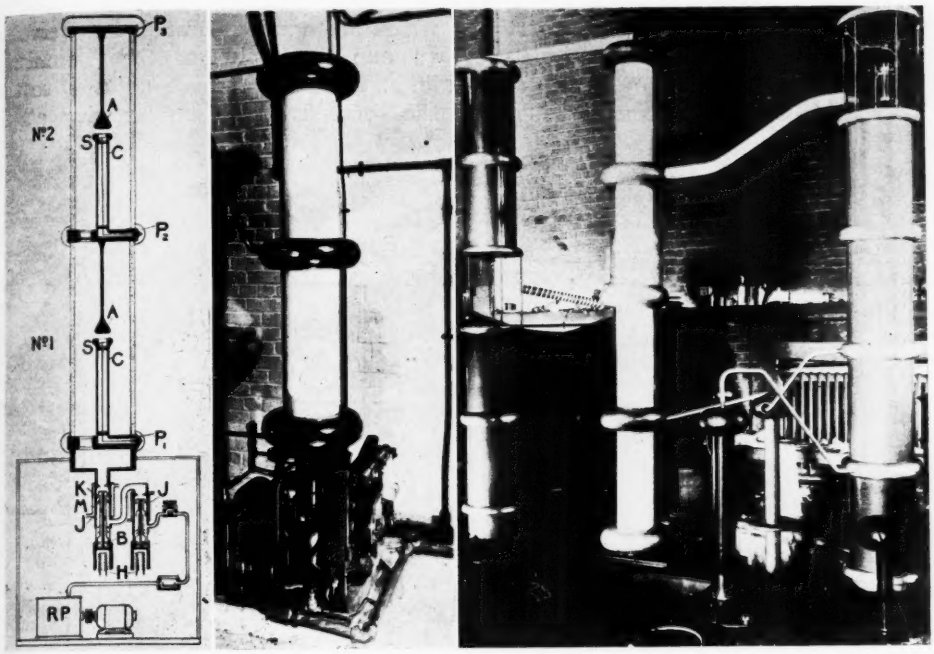

Fig. 5. Continuously evacuated thermionic rectifier for 300 kv. At the left may be seen a diagram and photograph of such a rectifier; at the right, its use in a Cockcroft circuit to give 600 kv. D.C. (smooth) and 10 ma. (Courtesy of Metropolitan-Vickers Electrical Company, Ltd.)

(4) *Radio-oscillator IIigh Voltage Roentgen Generator.*—This apparatus, which was devised by Sloan (9), occupies a place entirely apart, since it produces roentgen rays at very high voltages by the use of a radio-frequency resonance transformer in a vacuum tank which serves at the same time as the roentgen tube. Such an installation has now successfully been used for a period of over one year in the range of about 800,000 volts for the medical treatment of patients. The construction of this apparatus, the general layout of the treatment unit, as well as the type and characteristics of the radiation obtained, were published in detail recently by Stone, Livingstone, Stanley, Sloan, and Chaffee (10).

A new suggestion, merely on a theoretical basis, was made in connection with doubling up the energy of electrons in such a type of roentgen outfit by Du Mond (5), who advocates a sort of magnetic reflection arrangement. According to Du Mond's proposed technic, the electrons emitted from the high voltage terminal of the Tesla coil are accelerated into a field-free space, focused by a magnetic "lens" on a magnetic "mirror," then reflected back and refocused by the same magnetic lens on a target adjacent to the cathode and supported by the free end of the Tesla coil. It would be possible to obtain in this manner electrons impinging upon the target with an energy of 2,000,000 volts, the device thus permitting the generation of extremely hard roentgen rays. It must be stated, however, that the method has not as yet been tried out in practice.

(5) *High Voltage Impulse Generator with Multiple Acceleration on Transmission Lines.*—Another method which is likewise in the experimental stage, but may be mentioned because of its medical possibility, is that of Beams and Snoddy (3). This method consists in accelerating the electron by an electric field which is so adjusted as to move with approximately

identical speed. The discharge tube through which the electron moves is provided with short hollow cylindrical electrodes, each connected to a transmission line of increasing length but of very small "loading" or "tapering." The electric source is furnished by a Van de Graaff generator or Marx circuit in the form of surges or impulses, which are produced by the discharge between two metal spheres or more recently by an over-volted vacuum spark gap and which are applied simultaneously to all transmission lines. In this manner, the electron moving with the approximate speed of the surge or impulse on the transmission line is continuously accelerated by passing through the successive pairs of electrodes. The last apparatus which was published by Trotter and Beams (11) has seven transmission lines, the first terminating in a point wire, and the remaining one being connected to the successive electrodes mounted coaxially with the wire in an evacuated glass tube 4 meters long. The electric source is constituted by a generator making use of the Marx (7) circuit, the impulses of which are applied through an overvolted vacuum spark gap to the transmission lines. These latter are adjusted so that the successive impulses arriving at the respective electrodes first pull electrons out of the pointed wire and then accelerate them between each pair of electrodes. In this way, it was possible to obtain electrons of 2,500,000 volts maximum energy from a potential of 540,000 volts Marx circuit, which in turn was supplied with only 45,000 volts initial potential.

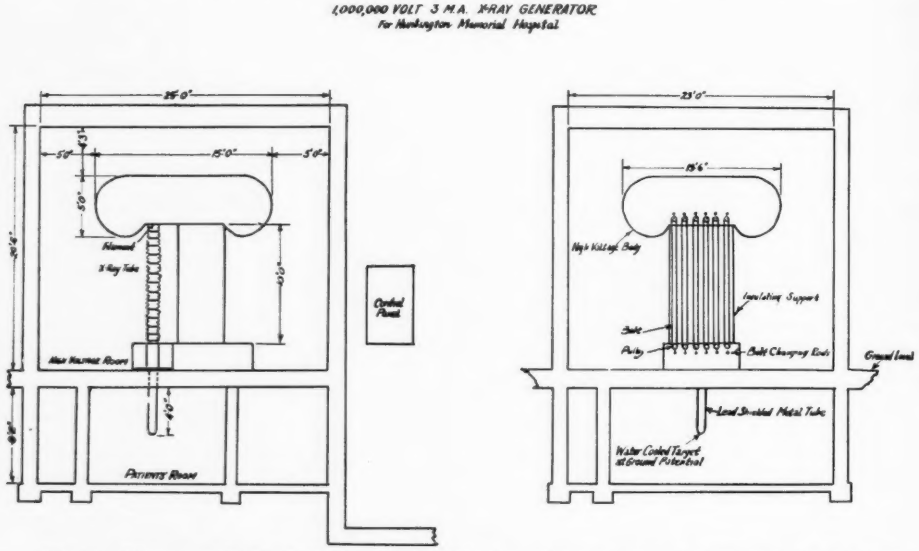

Fig. 6. Diagram and plan of the Van de Graaff static machine to be installed at the Collis P. Huntington Memorial Hospital, to operate at 1,000 kv. and 3 ma. (Courtesy of Dr. Richard Dresser and Mr. John G. Trump.)

(B) SUPERVOLTAGE TECHNIC FOR ACCELERATION OF IONS

In a manner similar to the acceleration of electrons, high voltage technic may be used also for the acceleration of ions. Although such a procedure has nothing to do with roentgen therapy, it is incorporated briefly in this paper because of its possibility in the treatment of cancer and other medical lesions.

It was brought out in our first paper two years ago that ions may be accelerated either in a straight forward fashion (by any of the methods described in the previous

paragraphs), or in a revolving manner by a system of multiple accelerations, according to Lawrence and Livingston (described in the former paper). Since that time the technical improvement has been of formidable proportions, and there are now a number of apparatus in actual use, some of them operating at voltages as high as ten million. It would exceed the purpose of this paper to enter into a more detailed consideration of the development of apparatus of this sort. Suffice it to say that the accelerated ions in the course of nuclear bombardment, for the prime purpose of which such apparatus are designed, give rise among other things to two phenomena which are of direct interest to medical investigation: the production of neutron rays and the artificial radio-activity. If both of these can be obtained in sufficiently large quantities for practical purposes, we may venture the following prediction concerning the possibility of their use:

(1) The neutron rays may be applied directly, the same as other types of radiation, for the treatment of cancer. Since they set free recoil protons from hydrogen, and since cancer, and the human tissues in general, are very rich in hydrogen, one can not conjecture enough about their therapeutic efficacy.

(2) Radio-activated salts (as, for example, table salt) may be injected locally into cancerous growths or into the blood-stream for a more generalized effect.

(3) Radio-activation may be produced in drugs with a more specific or more selective effect, permitting a radio-active influence limited to certain organs (liver, kidney, heart, etc.). This sort of treatment may prove of greater value to other lesions than cancer.

(4) Induced radio-activity in certain elements (Na, P, Fe, etc.) may permit the study of the exact metabolism of these elements in the system by measuring with some very sensitive instrument (the Geiger counter) the distribution of the elements in various parts of the body in normal and pathologic conditions.

There are probably other fields in which the use of neutron rays and artificial radio-activation may be of benefit, but which cannot be foreseen at the present time. An apparatus for the purpose of the investigation of these medical problems is now being installed in the Radiologic Department of Harper Hospital, under the direction of Dr. Evans and Dr. Reynolds, and is nearing completion.

CONCLUSIONS

There can be little doubt that the use of increasingly higher voltages is making rapid headway in the medical field. The apparatus used for practical roentgen therapy in the range above 200 kv. are becoming standardized. Where the new limits will lie is as yet difficult to estimate, but for the present it appears that the increase of voltage to from 400–600 kv. (equiv.) has, in certain instances, a decided advantage above the irradiation with 200 kv. On the other hand, the introduction of the neutron rays and artificial radio-activity in the medical field may make the use of considerably higher voltages, or their equivalent energies necessary.

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HEREDITY AND RADIATION[1]

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IT can hardly be doubted to-day that the laws of heredity, known as the Mendelian laws, are universal biologic laws. They have been found to hold true for all groups of living organisms which have been tested experimentally. These tests covered a wide range of organisms—in the animal kingdom: protozoa, molluscs, crustacea, insects, fishes, amphibia, reptiles, birds, and mammals; in the plant kingdom: bacteria, fungi, algæ, mosses, ferns, grasses, and a large number of orders of higher plants. Even though experimental breeding could not be carried out on human beings the statistical analysis of hereditary characteristics present in various families shows beyond any reasonable doubt that these laws apply to man as well.

One important point brought out in genetic experiments is the fact that the fundamental hereditary laws remain constant for all living organisms, thus making it possible to generalize the results of experimentation on any one organism and also to use for these tests the organisms best suited for experimental purposes.

Since the hereditary laws apply universally it is evident that the mechanism responsible for these laws must be identical for all organisms. I shall, therefore, begin this discussion with a brief review of what is known to-day about this mechanism.

The responsibility for the transmission of an hereditary characteristic can be definitely traced to a minute particle present in the germ-cell, called a gene. For example, a gene difference is responsible for a white or a red eye color in the vinegar fly (*Drosophila*), or for short *versus* long wings, cut *versus* whole wings, no wings *versus* the presence of wings, etc. We do not say, however, that there is a particular gene in the germ-cell which determines the color of the eyes; another one which determines the size of the wings; still another, the shape of the wings, etc., *viz.*, that there is a gene in the germ-plasm for every organ or every characteristic of the organism. We know positively that this is not true. We know that the whole set of genes of an organism works as a unit and that it forms a balanced system which, together with the environment in which the organism develops, determines the appearance and the characteristics of the individual.

The total number of genes in an organism is large; in *Drosophila* it is estimated that there are between three to five thousand of them. If any change in a gene occurs, such a change is liable to upset the balance of the gene system and to have a detrimental effect upon the organism, which effect sometimes expresses itself as a definite morphological characteristic. That this balance of the gene system is a sensitive one is indicated by the fact that in a number of investigated cases in which either one or a very few genes were missing from a fertilized ovum, such deficiencies affected physiologic processes of the developing organism to the extent of being lethal. Detailed studies of certain of these deficiencies revealed that they have a lethal effect on even a small patch of cells which is surrounded by otherwise normal tissue. This indicates that genes perform very important functions, not only for the organism as a whole but also for every individual cell of that organism.

It is known that genes are ultramicroscopic particles, probably single organic molecules, that they are very stable, and that they possess the power of self-reproduction which is the most important property of living matter. Every cell of an organism possesses a large number of such particles—in the case of *Drosophila* over

[1] Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, at Detroit, Dec. 2–6, 1935.

three thousand different ones, which perform a highly important function which in many instances is vital to the cell.

Genes behave as highly stable entities. Although changes in genes do occur, they are very rare. There is ample evidence to show that genes are not affected by ordinary environmental factors, *viz.*, that the ordinary environment is ineffective in producing hereditary changes. That does not necessarily mean that genes are chemically highly stable particles. It may indicate only that they are well protected by other components of the living cell. The only effective agencies in producing changes in genes are those which are able to reach the gene without injuring the cell. The most effective ones are x-rays and related radiations, which invariably produce changes in genes (Muller and others). Ultraviolet rays are effective also, but because of their low penetration they can be applied only in specific cases (Altenburg, 1934). High temperature is the third environmental agent known to affect genes; however, it also can be used effectively only in special instances (Goldschmidt, 1929; Jollos, 1930; Plough and Ives, 1934; Buchmann and Timoféeff-Ressovsky, 1935).

Experimental evidence indicates that over 80 per cent of detectable changes in genes eliminate the gene (Demerec, 1933), *viz.*, produce gene deficiencies. Such gene eliminations may be visualized as due to the loss of the reproductive power of the gene. Genes without reproductive capacity are automatically removed from the gene complex during the first cell division after such a change has occurred. As has been mentioned earlier, the great majority of gene deficiencies are highly detrimental to the organism. Viable gene changes also disturb the balance of the gene system and are likely to be detrimental to a greater or lesser degree.

The hereditary changes produced by x-rays are of two types, *viz.*, changes in genes and various chromosomal rearrangements. A large proportion of these chromosomal abnormalities coincide with detectable gene changes, so that the possibility is not excluded that both of them are due to the same cause, *viz.*, that the chemical reaction, which takes place when a change in a gene occurs, affects adjacent chromosome threads in such a way that they fuse together and a rearrangement of sections occurs at the time when they break apart again (Demerec and Lebedeff, 1935).

The effect of the quality of radiation on the frequency of hereditary changes has been extensively tested by various workers (Efroimson, 1931; Hanson and Heys, 1929; Stadler, 1931; Timoféeff–Ressovsky and Zimmer, 1935). Their results show conclusively that the quality of radiation, within the range tested (about 0.02 Å. to about 2.10 Å.), had no significant influence on the frequency of gene changes. It would be of theoretical interest from several standpoints to carry on these tests with still longer wave lengths and to make an exact comparison of the effects produced by ultraviolet rays and by x-rays.

The results of numerous experiments on the relation between the dosage and the rate of genic changes show that the rate of changes increases proportionally with the dosage applied. Some of these experiments are summarized by Timoféeff-Ressovsky (1934) in the chart shown in Figure 1. The data indicate a simple relation between the electron hits and the changes produced in genes. This relationship is further indicated in the evidence obtained in fractional treatments. Patterson (1931) treated six sets of *Drosophila* males with 1,220 r units; one set was treated continuously and in the other five sets treatment was applied in eight fractions, the intervals between fractions being 24, 12, 8, 1 and $^1/_2$ hours, respectively. Timoféeff-Ressovsky (1934) applied a dosage of 3,600 r units in six fractions spaced at 24-hour intervals. In neither of the experiments did fractioning have any influence on the induced mutation rate. These results show that there is no "recovery" in the case of hereditary effects and suggest that the electron hits produce changes in genes directly, since it is known that such changes, once

they have occurred, do not revert back. By increasing the dosage applied to a certain set of genes, therefore, the chances of a gene being hit by an electron are increased irrespective of whether the increase in dosage is accomplished through a longer continuous or fractioned treatment.

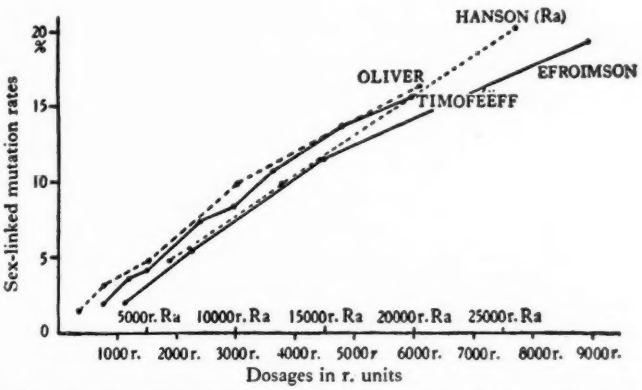

Fig. 1. The proportionality of the rates of sex-linked mutations in *Drosophila melanogaster* to the dosages applied. X-ray experiments of Timoféeff-Ressovsky, Efroimson and Schechtman, and Oliver, and radium experiments of Hanson and Heys. (*From Timoféeff-Ressovsky, 1934.*)

X-rays are a very effective agent in producing hereditary changes. An application of about 2,000 r units increased the natural rate of gene change in *Drosophila* about one hundred times. In an experiment in which *Drosophila* sperm were treated with approximately 2,500 r units (Demerec and Lebedeff, 1935), out of one hundred sperm tested for x-chromosome changes, eighteen had lethal and visible gene changes and five had chromosomal rearrangements. Since the x-chromosome constitutes less than one-fifth of the total volume of the chromosomal set, these results indicate that more than one hereditary change per sperm should be expected from a 2,500 r unit treatment, if changes occur with equal frequency in other chromosomes. All of the changes observed, both genic and chromosomal, were detrimental to the organism.

As has been mentioned earlier, one of the basic concepts of genetics is that a full complement of genes is present in every cell of an organism. The logical sequel of this concept is that changes in genes may occur in any cell of the organism, but only those affecting the reproductive cells will be transmitted to the offspring. It should be expected, therefore, that x-ray treatment of somatic cells would produce genic changes similar to those obtained from treating germ-cells. This is exactly what was found to happen. Patterson (1929) x-rayed eggs and larvæ of *Drosophila*, and observed on adult males distinct patches showing the characteristics of genic changes. These patches varied in size according to the stage of development at which the treatment was applied. The treatment produced a change in a gene of a somatic cell and if it were given early in ontogeny, the cell with the changed gene divided many times, producing a large spot, but if the treatment were given late in ontogeny, the affected cell passed through a few divisions only, producing a small spot.

The effectiveness of x-ray radiation in producing hereditary changes has been demonstrated on a large enough group of organisms to make it certain that x-rays are generally effective in producing such changes. According to Timoféeff-Ressovsky (1934), the following organisms have been used in genetic radiation work: (*a*) Protista: *Chilodon* (MacDougall); (*b*) plants:

Nucoraceæ, Sporobolomuces, Nadsonia (Nadson and Philipov), wheat (Stadler, Sapchin, Delanny), oats (Stadler), barley (Stadler), rye (Levitsky, Navashin), *Hyacinthum* (de Mol), *Nicotiana* (Goodspeed), *Datura* (Blakeslee), tomatoes (Lindstrom), *Mirabilis* (Brittingham) and *Antirrhinum* (Stubbs); (*c*) animals: *Apotettix* (Nabours), *Bombyx* (Astaurov), *Habrobracon* (Whiting), *Drosophila melanogaster* (Muller and others), *D. funebris* (Timoféeff-Ressovsky), *D. pseudo-obscura* (Schultz), *D. virilis* (Demerec, Fujii), *Macrosiphum* (Pirocchi), and mice (Dobrovolskaia-Zavadskaia, Snell).

I shall conclude this presentation by expressing a geneticist's opinion concerning x-ray treatment of human beings. A geneticist would not oppose treatment applied to somatic tissues. It is true that such treatment produces genetic changes similar to those produced by the treatment of germ-cells, but it is very likely that the organism will take care of detrimental genetic changes produced by it. In the treatments of somatic tissues, however, difficulties might arise if the application is given to fast-growing tissues or to embryos. In these cases cells possessing induced detrimental genetic changes might multiply and develop into sectors of abnormal tissue with a possible detrimental effect to the individual. A geneticist, however, would strongly oppose the treatment of any cells which would develop into functioning germ-cells. Experimental research has positive evidence to show that such treatment increases the frequency of hereditary abnormalities. Some of these can be expected to be so great as to produce abnormal embryos which would be eliminated before birth; others would develop into abnormalities which would show up on the offspring of treated individuals; the majority of these abnormalities, however, would be recessive and would not appear in the first generation offspring, but would crop up in later generations if mating should bring together two germ-cells carrying similar abnormalities. A geneticist would not hesitate to predict that indiscriminate x-ray treatment of germ-cells will increase the number of carriers of detrimental hereditary characteristics in any race in which that treatment is practised, and if continued long enough, will have a grave detrimental effect on the race as a whole.

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DISCUSSION OF SYMPOSIUM[1]

DR. MILTON FRIEDMAN (New York City): Each one of this mornings' essayists has indicated discrepancies between his own results and those of the other speakers. Therefore, it is not too great a presumption to introduce clinical facts and variables which re-emphasize the difference in the biologic effect of varying wave lengths.

Firstly, x-ray burns are not infrequently followed by cancers, whereas, on a radium burn, they are relatively uncommon.

Secondly, it has been established by us and by others, that if a full erythema dose is given at one time with x-rays produced by 200 kilovolts, and filtered with 0.5 mm. copper, the erythema will appear on the twelfth to the fourteenth day, whereas, if a single erythema dose is given at one time with a heavily filtered radium pack (in our case, 3 mm. of platinum), the erythema will not appear until the fourth or sixth week and sometimes even later. This profound difference is frequently overlooked in comparing these various radiations.

At Bellevue Hospital we are now in our fourth year of comparing different wave lengths in the treatment of neoplasms of the mouth and throat, with protracted radiation—which protraction brings out the delicate differences between different types of radiations to a great extent—more so than single individual doses—and we too have learned, as Coutard originally stated, that x-rays filtered through 2 mm. of copper are more effective than those filtered with 0.5 mm. of copper. If the intensity factors are equal, the skin can tolerate more of the shorter wave length radiations, in a ratio of approximately eight to seven.

GIOACCHINO FAILLA, D.Sc. (New York): I just want to mention one point in connection with Dr. Friedman's discussion, because it may lead to serious consequences.

Dr. Friedman mentioned that there have been no cases of cancer developing from over-dosage with radium. As a matter of fact, I know of some definite instances in which cancer has developed from radium burns in the hands of physicists and radiologists.

DR. CHARLES B. WARD (Seattle, Wash.): The skin reactions following the use of 800,000 volts x-ray, filtered through the equivalent of three millimeters of lead, have been very interesting. By using a divided dose technic we could occasionally give 5,000 r to a single port—we sometimes could go up to 6,000 r if we used a small port. This dosage produced no serious skin reactions on the neck but when the same amount of treatment was given over the jaw or antrum, the reaction was far too severe. A similar effect was noticed in treating a thin patient over the sacrum. This finding would tend to support Lauritsen's contention that the difference in distribution of secondaries is the main factor in minimizing the skin damage with supervoltage x-rays.

We also made tests for threshold erythema at various voltages and with filtration varying from five millimeters of copper to the equivalent of three millimeters of lead. We noted that as the filtration and voltage increased the time interval before the appearance of the skin pigmentation was also increased, and it was necessary to extend observations over a longer period of time. I believe that this delay in skin reaction is due to a difference in the quality of the radiation.

CHAIRMAN WOOD: We might ask Dr. Ward if he could give that supplementary information concerning the concrete and lead.

DR. WARD: Although I am no longer connected with the Swedish Hospital, I will be very glad to give you some preliminary data regarding the comparative protective value of concrete and lead.

[1] The papers of P. S. Henshaw, Ph.D., G. Failla, D.Sc., Prof. H. Holthusen, M.D., L. S. Taylor, Ph.D., and S. G. Mudd, M.D., with C. K. Emery, M.D. and R. S. Harrison, M.D., have not been received for publication.

Three years ago I was in Brussels. They have a very large supply of radium on hand in a lead-covered safe. This safe is placed in a room which has concrete walls one meter in thickness, and you enter this room through a winding passage.

Some months later we went over the General Electric specifications for the 800 kv. tube and found that they called for three inches of lead in the floor of the treatment room, two inches in the side walls, and partial leading of the control room and transformer room. I suggested concrete as a substitute. Some tests were made at Memorial Hospital and we finally decided to use three feet of concrete in the floor of the treatment room instead of three inches of lead, thirty inches of concrete in the walls of the room instead of two inches of lead.

After treatments were started, dental films were placed in various parts of the building for two weeks at a time. No fogging could be detected under the floor or outside the walls of the treatment room. These tests were repeated several times. At the present time Mr. J. E. Rose, the physicist at the Swedish Hospital, is making very complete tests which will be published in the next few months. He tells me that three feet of concrete is many times as efficient as three inches of lead. If any of you are considering such an installation, I am sure that you can feel safe in using concrete. Mr. Rose's data will be available at the Bureau of Standards in a very short time.

Dr. Roscoe L. Smith (Lincoln, Nebr.): I first adopted the use of voltages higher than 200 kv. in the Summer of 1933. Since that time 350 tumors have been treated, either by supervoltage alone or in combination with radium and surgery. Prior to 1933, I used a similar combination with 200 kv. Certain observations as to the effect of higher voltages must, therefore, be compared with my previous experience, using the same combinations but with lower voltages.

During the time of our experience with higher voltages the filtration and voltage have been increased from time to time, each step showing some improvement in the various effects that I will mention, the best effect occurring during our last and present setup.

72 cm. distance	plus	3 mm. steel
2.2 mm. lead filter	original	3 mm. Al
0.5 mm. copper	filter	9 mm. water
0.25 mm. block tin	in tube	
3 mm. celluloid		

700 kv. C.P. electro-static voltmeter reading
Output, 15 r per min.
Daily dose, 300 r
Total to one skin field, 2,000 to 3,000 r through multiple skin fields.

Although the subject is open to controversy it is my opinion that supervoltage radiation is superior to 200 kv. radiation for the following reasons:

(1) Pre-operative radiation of this type is of great advantage on early cases and surpasses other palliative measures on incurable lesions.

(2) More rapid tumor regression is noted.

(3) There is rapid relief of pain.

(4) Radiation sickness and skin erythemas are absent.

(5) Blood changes are less severe.

(6) The general condition of the patient improves more rapidly and the improvement is more apt to be permanent.

(7) In my experience long protracted treatments of supervoltage are most desirable.

(8) A combination of extremely high voltage radiation and one-third of an erythema dose of lower voltage treatment seems to produce more rapid recessions on diffuse, superficial lesions.

(9) The effect on neoplasms closely resembles the changes produced by interstitial radium radiation. It is not uncommon to observe in sections of previously irradiated tumor tissue a complete destruction of the nucleus where only the cell walls remain visible. In others there is a varying degree of pycnosis and the cytoplasm is distended with a clear, pale staining substance. Many times the cytoplasm becomes granular and there is marked karyorrhexis. Even when such damage occurs to

the bulk of the cell mass there are as a rule scattered clumps of cells which, as judged by their staining characteristics, appear viable, although there is definite evidence of severe damage.

No attempt has been made to measure depth dose since we believe the measurement of depth dose is as yet impractical. It is our purpose to produce the best quality of radiation possible, by high voltage and dense filtration, with adequate focal skin distance, and deliver sufficient radiation to cause a favorable reaction.

Whether the improvement in results is due to the quality or quantity of radiation delivered to the tumor is undetermined and is, I think, a problem for the future.

I have a few lantern slides which show some developments made on higher voltage apparatus at the Lincoln General Cancer Clinic by T. R. Folsom, in charge of the Department of Physics.

First: Our measurements are made by a large open air chamber placed on the outside of the treatment room and protected by a two-foot wall of concrete. A small beam of x-ray is allowed to pass through a lead gate in the wall to the air chamber. Through a tunnel on the opposite side it escapes into the ground, thus avoiding any back-scattering. The position of the standard air chamber is approximately eight feet from the focal spot of the tube.

Second: Dr. Leucutia has brought out some points concerning vacuum pumps. In the beginning we used mercury vapor pumps similar to those described by Dr. Leucutia. They were a constant source of trouble and expense. After a few months of unsatisfactory experience, Mr. Folsom built our first set of apazine oil pumps; these were located about twelve feet from the tube. Several attempts were made to obtain satisfactory operation but it was not until a new set of pumps were located only a few inches from the tube proper that we were able to get satisfactory and rapid evacuation.

Third: The x-ray tube, in the beginning, was similar to that used by Dr. Leucutia, end ground and one stage. We experienced considerable difficulty operating over 400 kv. For this reason the tube was rebuilt into a two-stage affair, which permits operating at capacity.

About this time the small one and one-quarter inch gold target was abandoned. Mr. Folsom substitued a target three and one-half inches in diameter, constructed of $^1/_{100}$ inch pure lead on a copper backing. This has not only reduced the replacement cost from $40.00 to $0.50 but has increased our efficiency output and quality of radiation.

Fourth: The entire end of the tube has been remodeled and for the brass water jacket, one of aluminum has been substituted. This change has been of the greatest advantage in equalizing the quantity and quality of all four ports. The output from each is now not only equal in volume but equal in quality as well.

Fifth: The cone construction has also been changed. We have installed cones of one-half inch lead, lined with aluminum, with a rotating cap, which permits selecting any sized opening at any desired angle.

An electric light bulb has been placed in the extreme apex of the cone, the light permitting the operator to determine the exact location, size, and shape of the area to be treated. There has been (and justly so) criticism on the difficulty encountered in securing proper positions with a fixed tube. We find with our present setup that it is sometimes difficult to secure correct areas. The light, however, assists us materially and affords an accurate means of determining the tissue which will receive radiation.

The voltage referred to in the above discussion was checked on each individual transformer, later by the large sphere gap and again by the electro-static constant reading voltmeter. Needless to say, these measurements may be in error and are subject to future correction.

DR. HENRY SCHMITZ (Chicago): [The Editor wishes to state that Dr. Schmitz wished to combine the discussion he presented in this sequence with his paper, the latter to be published at once (March, 1936,

26, 331–334). This was done at his request.]

DR. WILLIAM E. COSTOLOW (Los Angeles, Calif.): The problem of determining the clinical value of supervoltage irradiation presents many difficulties, as does the determination of the value of the biologic and physical measurements which we heard about this morning.

Erythemas have been mentioned. I will briefly state our experience. It was brought out this morning that in the production of an erythema by a single dose, a larger dose was necessary, and that the erythema came on at a later date when the supervoltage was used than when 200 kv. was used. This is perfectly true, but by fractionating the dosage over a period of five to six weeks, this difference is very difficult to detect. For instance, in treating the pelvic conditions with supervoltage in cases in which we use as many as six portals, giving a total of from ten to twelve thousand r units over a period of five to six weeks, as compared with the same sort of cycle with 200 kv., applying the same total dosage in r (measured in air) over the same period of time, the erythema is very similar in its appearance and disappearance, and the condition of the skin several months later seems practically the same.

We have had the opportunity of observing the use of 500 kv. with 0.6 mm. of lead filtration at our own office, and also the use of the 900 kv. with 1 mm. lead filtration, at California Institute of Technology. We use the same r intensity per minute, and if we use the same size fields, daily dosages, and total days of treatment, the skin reactions produced by the two machines are apparently quite similar.

Definite proof of the superiority of supervoltage, if any, will come only after five years, or longer periods of observations. The only factor we can use now for basing any sort of comparison on, is, as Dr. Schmitz has mentioned, the matter of the primary regression of the tumor. This is quite difficult to determine clinically. It is quite inconclusive to compare the results in groups of cases treated in the past, in which the total dosage and time of treatment were less, with the results of the larger fractionated dosages now given.

We must not forget the work that Dr. Coutard and his associates have done in the pelvis with 200 kv., using large, prolonged, fractional dosages over multiple portals and obtaining disappearance of pelvic gland metastatis, which simulates any primary regression so far obtained with the supervoltage.

In our pelvic cases we are getting better primary regression since using the supervoltage. This may be because we are using larger dosages than formerly. It is pretty difficult to compare the supervoltage results with work done previously with 200 kv., so the apparent improvement may be more a matter of total dosage than we think. However, the question was brought up a minute ago as to whether we had treated any cases with supervoltages which had previously been treated with 200 kv. We have. Some of our old cases came back with recurrences after having had what we considered, at that time, adequate radium and x-ray dosages. We have had complete regression in some of these cases after thorough supervoltage treatment. These results are, of course, encouraging, but the cases are few, and, in the past, striking primary results were at times noted, following other forms of irradiation, although apparently not so frequently as at the present time. One thing we may say: that the supervoltage offers a method by which we can give the patient a very thorough course of irradiation. While it appears that we are getting better primary regression, I feel that we had better do as the physicists and biologists all did this morning—beg off from making any definite statements until more time has elapsed to permit further observations.

DR. L. S. TAYLOR (Washington, D. C.): I would like to ask Dr. Costolow what his alibi is when it comes to measuring these irradiations in roentgens.

DR. COSTOLOW: Our dosages are all measured by the same method used at California Institute of Technology—with the standard air chamber, the output in air being measured each morning.

DR. JOHN T. MURPHY (Toledo, Ohio): We have heard much this afternoon about the supervoltage from 550,000 volts to 800,000 volts. What I have to say will be based on 400 kilovolts of pulsating current.

The reason I adopted this machine was twofold: I could not afford a larger one and I thought somebody should try middle-volt radiation rather than the so-called supervoltage.

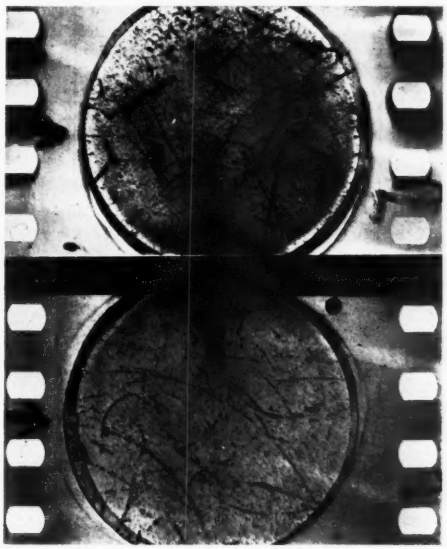
The factors I am using are 400 kilovolts pulsating current; 80 centimeters distance; filter, 2 millimeters of copper built into the tube and an additional Thoreaus filter of one-quarter millimeter of copper, four-tenths of tin, one of aluminum. The intensity varies with the tubes from 14 to 16 r per minute.

Of course, this machine has been in use for only eleven months and no final results can be told.

I am surprised that the men using higher voltage and higher dosage on the pelvis have so few complications. I cannot understand it because one of my great troubles is the care of the patient during the treatment from the mucosition produced in the bowel and other complicated effects both in the bladder and in the rectum. Whether this is because of a difference in biological effects, I do not know, but personally I have a great deal of trouble in controlling these elements.

We have nausea, even though we never go beyond 210 r per day per field and one field per day. We have weakness. We have diarrhea. We have trouble with the skin and I cannot understand, myself, why a machine that will produce the estimated depth dose of a machine at 800,000 on a patient 21 centimeters thick, does not produce complicating effects on the opposite skin portal.

DR. ROBERT R. NEWELL (San Francisco): In the first place, Dr. Leucutia has been looking into the future and talking about machinery for doing neutron production and nuclear reactions and artificial radio-activity and I am very fortunate in living just across San Francisco Bay from the first of the cyclotrons. I went over and borrowed from Professor Ernest Lawrence a couple of Wilson cloud chamber pictures. These are the original films he took with his Wilson chamber and he



let me have them to show you some of these reactions.

This first one is the result from radio-active sodium produced by bombarding common salt with high speed deuterons from his cyclotron. This breaks down into sodium again with the release of a high speed beta particle swifter than those from radium and a very hard gamma ray, harder than any from radium or thorium.

These gamma rays came in here [pointing] and released some secondary beta rays. The curvature in the strong magnetic field through the Wilson chamber indicates its energy, which is seen to be extremely high because it is not very much curved. In the other film, we have some deuterons allowed to bombard beryllium,

and the nuclear reaction has resulted in ejection of neutrons.

Neutrons and β rays are not absorbed by the same mechanism. A neutron is without charge and runs through matter without being deflected or jostling the electrons at all; when it runs head-on into a nucleus of an atom, then it gives a transformation and you get a recoil ion, and these latter produce very intense ionization tracks, as shown in this Wilson cloud chamber photograph.

Now I am very much interested in the minute mechanism of absorption of radiation within the human body, and when we compare the way a high speed electron is absorbed and the way a neutron is absorbed, we see that this [pointing to the track of the electron] is more or less like running a man through with a rapier. You can stick a man through the lung with a rapier and he may recover. But if you stab him with a flagpole [pointing to the recoil ion from the neutron absorption], I don't think he is going to recover at all.

So that I see some chance for selective action, some cells succumbing and some cells recovering (cancer being killed and normal cells recovering) when you use the secondary high speed electrons from photons (gamma rays or x-rays). But I do not see the medical use of neutrons when their ionization tracks are going to be so intense that you cannot imagine such a track going through a cell without killing the cell utterly, whether it is a cancer cell or a normal cell.[2]

GIOACCHINO FAILLA, D.Sc. (New York): I should like to bring out a point in Dr. Holthusen's paper which perhaps might be misunderstood. Dr. Holthusen did not present the erythema dose curve to show that there is no difference between x-rays and gamma rays, or, in other words, to show that there is no wave length effect, because his curve was not determined with the same quality of radiation.

In order to eliminate the wave length effect from the curve, it would have been necessary to carry out all the experiments with the same quality of radiation, whereas that was not the case, since some of the treatments were given with 500 roentgens per minute and some with one roentgen per minute, and it is difficult to see how one can get such a variation in intensity, without changing the quality of radiation, and perhaps some other factors.

Therefore, the curve really shows the combined effect of prolonging the time and decreasing the wave length of radiation, in view of the fact that the short exposures were given with long wave length radiation, and the long exposures with short wave length radiation—possibly gamma rays.

In order to evaluate what part of the change is due to either factor individually, other experiments must be performed in which one or the other of the two variables is kept constant.

I think that this is in accord with Dr. Holthusen's ideas, but I wanted to bring it out definitely so that there would not be any misunderstanding.

DR. L. HENRY GARLAND (San Francisco): As one interested in the clinical aspects of radiation therapy it has been a pleasure to listen to some of the papers read this afternoon, especially that read by Dr. Emery (and also Dr. Costolow's discussion thereof). It seems to be generally agreed that we are not yet in a position to decide the relative merits of high voltage (200 kv.) and supervoltage (900 kv.) radiation. From observations on some of the patients treated with the 900 kv. apparatus at the University of California Hospital it is my impression that Dr. Costolow's conservatism is more than justified. Dr. Stone unfortunately could not come to this meeting but he seems to have the impression that there is little clinical difference in either the amount of erythema or the type of reaction produced with these two very different voltages. This does

[2] Note added in proof: Considering Zirkle's figures on fern spores killed by x-rays (Am. Jour. Cancer, March, 1935, **23**, 558–567), I think I ought to have said merely that I think neutrons are not very promising for the treatment of cancer.

not mean, of course, that he feels the clinical results from treating pelvic tumors are the same with both types of radiation. I do not think he has yet made up his mind on this aspect of the problem.

Dr. Taylor mentions that, with 200 kv. radiation, physical measurements suggest that the correct focal skin distance should be approximately ten times that of the tumor depth. In view of this suggestion and in view of the fact that supervoltage is beyond the reach of many of us clinicians at the present time, I would like to ask Dr. Failla if he thinks super-milliamperage would be a more economical and simpler answer to some of the problems involved.

Personally, I have operated an ordinary water-cooled 30 milliampere tube at 40 milliamperes for several hours, without apparent damage—using 200 kilovolts. Now if one could secure 50 or 60 milliampere tubes one could easily treat deep-seated lesions at target-skin distances of 100 centimeters as a routine measure. With such milliamperage the output with either 0.5 or 1.0 millimeter of copper filter would still be ample.

FRANK M. EXNER, M.A. (New York): May I ask how the measurements in roentgens at 900 kilovolts are made at San Francisco?

DR. GARLAND: Well, Dr. Stone has his machine calibrated by the physicists from the University of California and they think they are measuring similar roentgens.

Of course, like everybody else, they do not know, but they think they are measuring roentgens in air with 900 kilovolts.

LAURISTON S. TAYLOR (Washington, D. C.): Rather than present a discussion, I wish to make a short plea. We have listened all day until our heads ache about the difficulties in the measurement of supervoltage radiations. It is very unfortunate that so many of these installations, as they are put in, have to be installed in existing buildings and consequently have been cramped as to space and lay-out of auxiliary apparatus.

I think it is highly necessary that those doctors who are considering new installations for voltages above 500 kilovolts ought to be a little public-spirited at the same time and make provision for some auxiliary space near their tube where adequate physical measurements can be carried out.

That means perhaps a little room off to one side—not so small, but a room where you can avoid scattering—where you can set up standard ionization chambers and make measurements under conditions wherein the scattered radiation can be controlled.

When a supervoltage x-ray installation is being built new, it is a simple matter comparatively to make such provision. After the installation is completed, it is a very difficult matter to make such provision.

I feel that questions of the type that have been raised all day will soon disappear if we can just have facilities available around the country for setting up apparatus and making unambiguous measurements.

Unfortunately, at the present time our laboratory, which is somewhat looked to for information of this sort, has no facilities whatever for carrying out such measurements. We have to go to outside laboratories, choosing here and there those particular ones which are suited to our purpose.

If, however, the next half-dozen installations which are built have provision made in their installation for some reliable physical measurements, and better still, if a physicist is attached to their staff to make these measurements, I feel the questions that are worrying us so much to-day will be more speedily rectified and answered.

GIOACCHINO FAILLA, D.Sc. (New York): The question of depth dose has been raised several times to-day, or at any rate it has been implied that with these very high voltage x-rays the depth dose must be very high.

As a matter of actual measurement, the

depth dose is not very different from that with 200 kv. x-rays under the same conditions. So if the clinical results are better, the improvement cannot be attributed entirely to the increase in depth dose.

The foregoing statement, of course, is based on the present method of measuring depth doses, but I do not believe the present method is very good, and we shall have to wait until a better method is developed before we can say definitely what the depth dose is with the higher voltage x-rays and gamma rays. With the usual small chambers, having thick walls, there is surprisingly little difference in depth dose between 200 and 400 kv. x-rays.

PAUL S. HENSHAW, PH.D. (New York): Dr. Packard in his main presentation has referred to the literature and pointed out that a large number of different wave lengths of x-rays have been used on a variety of different biological test objects and that practically no results were obtained which indicate a differential wave length effect. While this is true, it would probably be worth while to point out that the majority of these were carried out with x-rays produced at from 50 to 200 kilovolts. Surely it will be necessary to investigate the whole range of wave lengths of penetrating radiations, x-rays produced at from 50 to 1500 kv. or more, before conclusions can be drawn.

For most of the investigations previously carried out, one ionization chamber was used to measure the radiation intensity and one test object was used to measure the biological effect. Recent results have shown that intensity measurements of different wave length radiations made with different kinds of ionization chambers may not agree. This tends to discredit statements about the wave length problem which are totally dependent upon ionization measurements. It seems to us that it would be more satisfactory to irradiate a variety of test objects with the different qualities of radiation and compare the relative effects produced in the different materials. This eliminates all ionization chamber difficulties and compares tissue reactions directly, which really is the main point of interest in this work. It is to this kind of procedure that we attribute the fact that we have been able to observe differential wave length effects.

Packard has used one test object—*Drosophila* eggs—and ionization chambers and has found that the same relative effects are obtained in the eggs and for the ionization measurements for x-rays produced at from 12 to 550 kilovolts. We note, however, from his printed reports that certain corrections are necessary in case of the longer wave length (12 kv.) radiations in order to make the results parallel. Among these is a correction of 6.7 per cent for differential absorption of the radiation at different levels in the *Drosophila* eggs, the greatest thickness of which is about 0.1 mm. While this correction is not large and would not change final conclusions to a great extent, I would like to know why Dr. Packard assumes that a correction must be made for the unequal distribution of radiation throughout the organisms. This question is raised because we have been able to produce killing in these organisms with alpha particles when it was known that the radiation did not pass to the center of the eggs.

CHARLES PACKARD, PH.D. (New York): Very soft radiations are so readily absorbed that their intensity is appreciably lowered after traversing even a fraction of a millimeter of tissue. Thus the nuclei on the under surface of the *Drosophila* egg receive less radiation than those on the upper surface. The average intensity was, therefore, calculated. The correction amounted to 6 per cent. If we had been wrong in our evaluation of the correction by even 20 per cent, that would have introduced an error of only one-fifth of 6 per cent, that is, about 1 per cent in the final result.

Dr. Henshaw has referred to his experiments with alpha rays which are wholly absorbed in the cells on the upper surface of the *Drosophila* egg. The egg is killed even though only a part of the cells composing it are injured. This is probably be-

cause the intensity of ionization is very great. In these conditions the destruction of protoplasm is complete, and recovery impossible. Zirkle has observed the same phenomenon in fern spores. For equal amounts of ionization, he finds that the effect of alpha particles is greater than that of x-rays.

CHAIRMAN FRANCIS CARTER WOOD, M.D. (New York): As a person interested in both the practical and theoretical sides, I hope that we will soon have some tests on patients actually using the Coutard method of the application of irradiation—irradiation given at from 3 to 4 r per minute over a long period. These radiations are all given rapidly, in ten- or fifteen-minute exposures.

It is very interesting to find out if, by doing what Dr. Coutard does—expanding that radiation over a couple of hours for each exposure—we would not get different results.

I have been interested in working the other way. I am treating a considerable number of patients with about 140 to 150 kv., with a half-millimeter of zinc, raising the skin-focus distance until the dose is something like 3 r per minute and then giving long exposures. There is not the slightest difficulty in giving 6,000 r on the skin of a patient in the course of a month without getting a severe burn and very frequently with total disappearance of the metastatic carcinoma—for usually these are breast cases—from the surface of the chest and in that way I can guarantee no fibrosis of the lung is produced.

These big machines do produce fibrosis of the lung, as is well known. In some cases the fibrosis has been more serious than the primary disease from which the patient suffered, notably, cancer. It is like shooting at a *Drosophila* egg with a 13-inch Navy gun to use a very high voltage in treating superficial lesions!

Why do we have to use a ray which will penetrate the chest and ray people a block or two away when the dosage can be so adjusted that we can apply a sufficient dose to the two or three centimeters of thickness of tissue that we are treating, provided we alter the dose so that it conforms to the factors which Dr. Holthusen's charts show. The difference between the various doses of radiation affords a very valuable and useful check on our radiation therapy.

When you see that with 5 r per minute you can give a very much larger dose of radiation and that the danger of serious damage of the skin is considerably farther from the erythema dose than when the rate is 500 r per minute, we feel very safe in giving six and seven hundred r, if so desired, without producing serious damage.

MITOSIS DURING THE HEALING OF X-RAY BURNS[1]

By JOHN A. CAMERON, M.A., PH.D., *Columbia, Mo.*

From the Department of Zoology, University of Missouri

CELLS lost by the epidermis after x-ray injury might conceivably be replaced through several processes. Mitosis of the remaining cells of the burned region is a method commonly described. Other possible means that have been described are amitosis (Kindred, 1927), lateral migration from nearby uninjured skin (Arey, 1932), modified mitosis (Stough, 1931), and migration and differentiation of cells of the dermis or of deeper layers of the body (Papanicoulaou, 1933, and Cameron, 1936).

In the present series of experiments square burns 6 × 6 mm. were made on the backs of frogs by the application of 1,000 r. X-ray exposures were made in the laboratory of Professor L. J. Stadler, of the University of Missouri, with a Victor machine (Snook model), having mechanical cross-arm rectifier and universal type Coolidge tube operated at 140 kv.p. Tube current was 4 ma.; target distance, 11 inches; time, 7 minutes, 24 seconds. No screen or filter was employed. Each frog was chloretonized during exposure, and the size and location of the injury were regulated by the size and position of a square hole in the lead plate that shielded its body. The output of 136.5 r per minute was measured with a Victoreen dosimeter. Each week for 10 weeks following irradiation a frog was killed and a square of skin 18 × 18 mm. which had the burned square as its center was fixed in Bouin's fluid. A control square was taken from each frog. Each piece of tissue was cut into serial sections 6 mμ thick and stained with Mayer's hæmalum and orange G.

[1] This study was aided by a grant from the Committee on Radiation of the National Research Council to W. C. Curtis.

In the distribution of mitotic figures and "travelling cells," no differences were found between specimens cut along the longitudinal and those cut along the transverse axes of the animals. A certain amount of shrinkage in the burned area resulted in some distortion of the cells around the periphery of the burn and in the drawing of neighboring cells out of the perpendicular in the direction of the center of the burn, but no evidence of lateral migration was found. The very low percentage of cells in mitosis detected in rapidly growing tadpoles made the modified mitosis described by Stough a very attractive explanation of the source of the new cells. Nevertheless, nothing indicating modified mitosis was seen in the slides; only normal mitoses were found, which suggests that the cells in mitosis were not present in the epidermis at the time of exposure to x-rays but have subsequently arrived from the deeper layers of the body.

One week after exposure the skin was reduced from six to five layers of cells; the control had three layers in the basal region in which metabolism was active but the irradiate had only two such layers. Many of the nuclei were swollen as though by excess fluid. The external layer of flattened cells was only loosely attached in the irradiate. In some of the sections the desquamated sixth layer was represented by long streamers of burned cells which dangled from the free border of the epithelium. After three weeks there were only four layers and all except the basal one were obviously undergoing degenerative changes. Among the old cells were some large, turgid, chromatic ones which appeared unaffected by x-rays, these being chiefly at places just external to the end-

ing of a vertical connective tissue fiber bundle. Sometimes a procession-like series of four or five such "travelling cells" could be followed away from the vertical bundle locus. At the end of five weeks most of the basal cells showed shrinkage of the nucleus and vacuolization of the cytosome. The contrast between these cells and those described as unaffected was very marked. The latter were now numerous and distributed along the whole length of the section although they were still more common near the vertical bundle terminations. At some points the epidermis was now only three cells thick. In the seven-week specimen there were at some places only two layers of epidermis but the basal layer was definitely on the way to recovery. The majority of the basal cells seemed normal and there was little vacuolization. The final sample, taken after ten weeks, showed three or four layers of cells with many of the normal type in the second and even the external layers.

The new cells which appeared at the site of the injury and formed part of the regenerating epidermis might be thought to be derived from mitotic divisions of the cells of the burned area or the zone just external to it which was included in the square of tissue examined. Counts of 10,000 cells for each specimen showed no significant difference between the number of mitoses in the irradiated and the control skin. These differences are shown in Table I.

TABLE I.—NO. MITOSES PER 1,000 CELLS

Weeks after 1,000 r	Control Skin	X-rayed Skin
1	14	12
2	5	8
3	20	25
4	20	26
5	16	19
6	24	20
7	26	22
8	12	15
9	11	13
10	12	15
Totals	160	175

In cases in which an open wound is present, the epidermis of the frog is first completed through lateral migration of epidermal cells from the surrounding region (Arey). In the present series there was no open wound. Lateral migration is not indicated by the slides, and the time of appearance of new cells is not related to their distance from the edge of the injury. New cells are found near the center of the burn as soon as at its edge, and not only at the surface but beneath the injured cells. Appearing first at the loci of vertical connective tissue bundles, they are found in positions indicating that they have migrated along the bundles from the deeper layers and joined the dermis. In the normal dermis the vertical bundles bear similar cells, but in the x-rayed tissue there is an average increase in their number of 50 per cent for the ten-week period, with a high point of 100 per cent for the third week following irradiation. Table II gives the weekly counts of these cells.

TABLE II.—"TRAVELLING CELLS" FOUND ON 25 VERTICAL CONNECTIVE TISSUE BUNDLES

Weeks after 1,000 r	Control Skin	X-rayed Skin	Percentage of Increase
1	198	266	35
2	190	278	45
3	188	400	113
4	260	350	45
5	185	263	40
6	145	250	83
7	155	375	77
8	218	278	26
9	186	224	20
10	178	201	18
Average	190	288	50

SUMMARY

The epidermis, which was reduced by x-ray injury to two layers, was restored to four or five layers in thickness without significant increase in the mitotic divisions found and with no evidence of amitosis. Travelling cells of the dermis were much more numerous during the period of regeneration. These findings support the idea of replacement of epidermal by dermal cells.

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CASE REPORTS AND NEW DEVICES

ENLARGED PARIETAL FORAMINA

REPORT OF AN ADDITIONAL FAMILY SHOWING THIS ANOMALY

By REUBEN G. ALLEY, M.D., *Pittsburgh, Pa.*

From the Diagnostic X-ray Department of the Western Pennsylvania Hospital

Probably every roentgenologist has a varying number of films that are filed in a special place, with at least a mental note to the effect that more information is desired regarding them. These may be waiting for biopsy or operation or may even be kept with the hope of finding a similar case that may shed light upon an unusual condition. Such a case of ours was brought to mind by the article of Dr. O. H. Perry Pepper and Dr. Eugene P. Pendergrass in the January "American Journal of Roentgenology and Radium Therapy."

In July, 1933, an eight-year-old colored boy was injured by an automobile and routine skull films were taken. These revealed large, symmetrical, rather oval defects located in the parietal bones, just to the right and left of the mid-line (Fig. 1). There was a definite bony septum between them. No other cranial ab-

Fig. 1. Fig. 2.

Fig. 1. Robert, aged 11 years, was the first patient showing enlarged parietal foramina.
Fig. 2. Mrs. B., mother of all the children, whose films are shown.

Fig. 3. Bessie, aged 14 years. Fig. 4. Lucky, Jr., aged 12 years.

normality was seen. When viewed in the stereoscope there was noted a gradual thinning of the parietal bone surrounding these defects; the skull was slightly large but showed no other

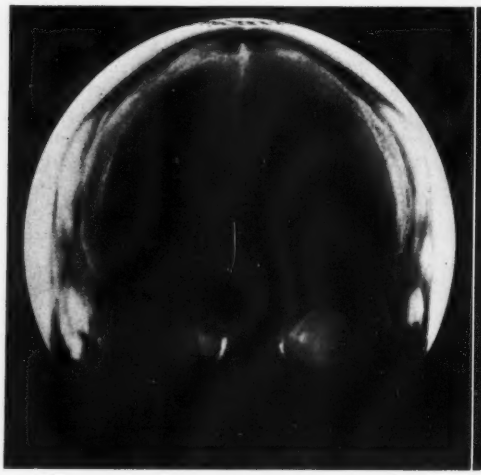

Fig. 5. Paul, aged 9 years a twin.

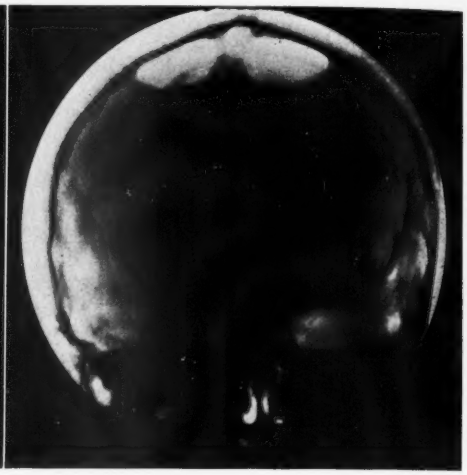

Fig. 6. Pauline, aged 9 years, twin sister of Paul (Fig. 5).

type of pathology or anomaly. There was obviously no relation between these areas of decreased density and the injury. Lack of scars ruled out any previous operative work, though had only one such area been seen, history regarding an old trephine would have been investigated. Metastatic malignancy could be eliminated in diagnosis because of the child's excellent condition and the lack of any primary tumor. Also, there were no palpable tumors associated with the bone lesion. The symmetry of the areas of decreased density, the smooth regular edges, and the lack of exophthalmos convinced us that Schüller-Christian's disease was not the causative factor. Syphilis was considered but eliminated by serology. Finally, a diagnosis of congenital bony defects was agreed upon. We considered the appearance unusual because no similar skull defects were located in our available literature, and though the writer had viewed more than two thousand skulls in this department, no other such case had been seen. So these films were kept out of our regular file, waiting for more information to be obtained regarding them.

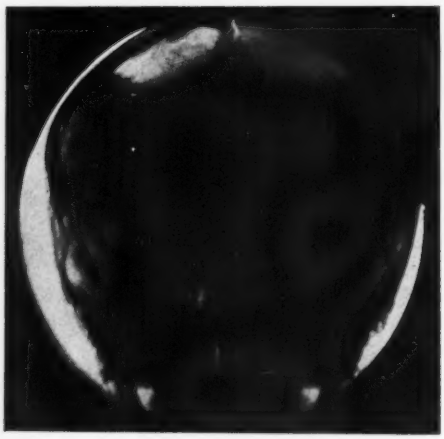

Fig. 7. Floyd, aged 6 years.

After reading the above mentioned article and also the references to "The Catlin Mark," by Dr. W. M. Goldsmith, in "The Journal of Heredity" for February, 1922, we were convinced that ours was a case of congenital enlargment of the parietal foramina.

On the posterior, superior aspect of the parietal bone, there is normally present a minute perforation that transmits a small vein to the superior sagittal sinus and at times a small branch of the occipital artery. Gray's "Anatomy" relates that this foramen may or may not be present and varies considerably in size; but even this did not prepare us to realize that the size could attain any such proportions as noted in our patient.

In brief, the points considered in diagnosing this case were as follows:

(1) The relation of these defects to the parietal bone;

(2) Their bilateral presence;

(3) The lack of symptoms in the patient;

(4) Palpable "soft spots" quite similar to the feel of a fontanelle;

(5) Their characteristic presence in other members of the family.

After making the diagnosis, we wished to confirm the previous reports of hereditary transmission, so we located this family and were able to obtain x-ray examinations of the mother and six children. No other relatives live in this State, but the mother has promised to bring to us any members of her family who may come up from Texas.

Films of this colored family are here shown. The mother (Fig. 2) has well outlined, enlarged foramina. They are less symmetrical and separated by a wider septum than noted on the first patient. The older girl (Fig. 3) has these defects, but they are smaller than her mother's. This girl is fourteen years old and in her second year of high school. All of the children are alert and very interested in their self-styled "soft spots." In fact, the oldest boy (Fig. 4) is very disappointed because he has none, and insisted that he have another x-ray examination to try to find that he was like his brothers and sisters. The twins (Figs. 5 and 6) are a very interesting study, and seem to prove that these enlarged foramina are no handicap to development. The girl has much wider defects, yet she is larger than the boy, appears older, though their mental development is approximately the same. The parietal foramen of the boy is indicated by an arrow on the film, for it is small enough to escape casual notice. The last film (Fig. 7) is of the six-year-old boy. The bony defects are very noticeable when palpating his head, but strangely, the mother had never noticed them until these examinations were made. The thick, woolly hair possessed by each member of this family has probably been a great protection. These children complain of no headaches or undue pain in ordinary childhood injuries.

These additional cases are reported solely for their value in differential diagnosis. There is, at this writing, only one article on the subject in roentgen literature and these films will increase our available references and make interpretation of similar skulls an easier process than our efforts in 1933. Apparently they are of no clinical importance beyond elimination of a real pathologic lesion.

OBSTRUCTION OF THE THIRD PORTION OF THE DUODENUM OF UNUSUAL ETIOLOGY

REPORT OF A CASE[1]

By LESTER W. BAIRD, M.D., Fellow in Radiology, The Mayo Foundation, *and* B. R. KIRKLIN, M.D., Section on Roentgenology, The Mayo Clinic, *Rochester, Minnesota*

Lesions producing obstruction of the third portion of the duodenum may be classified as intraluminal, mural, and extraduodenal. Obstruction may be produced by intraluminal lesions such as ingested foreign bodies and trichobezoars. Lesions of the mural type which may be responsible for obstruction include inflammatory lesions, benign and malignant tumors, and congenital stenosis. Since the third portion of the duodenum is retroperitoneal and crosses the vertebral column, it may be easily compressed by lesions in the surrounding tissues. Therefore, a large variety of extraduodenal lesions are comprised in this group, namely, congenital bands, particularly those extending between the transverse colon and jejunum; persistence of the anterior mesogastrium; adhesions to surrounding organs which are inflamed, such as the gall bladder,

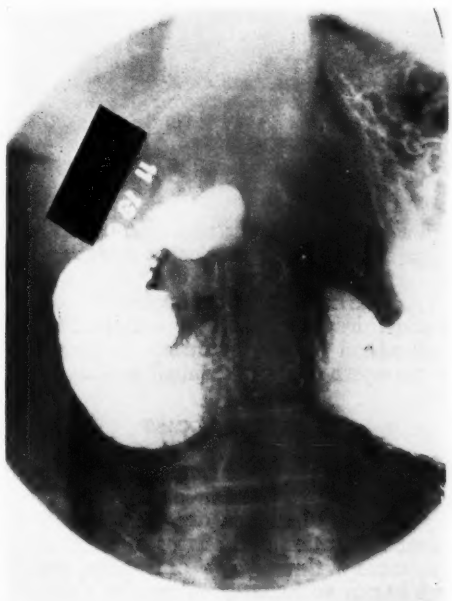

Fig. 1. Compression of the third portion of the duodenum and antral portion of the stomach by an extrinsic mass.

[1] Submitted for publication May 12, 1936.

stomach, or colon; lesions of the pancreas, particularly inflammation, carcinoma, or cysts; enlarged mesenteric lymph nodes, and, rarely, compression by the superior mesenteric artery in persons of asthenic habitus. Cases have been reported in which an enlarged spleen or liver, movable kidney, or abdominal aneurysm produced obstruction.

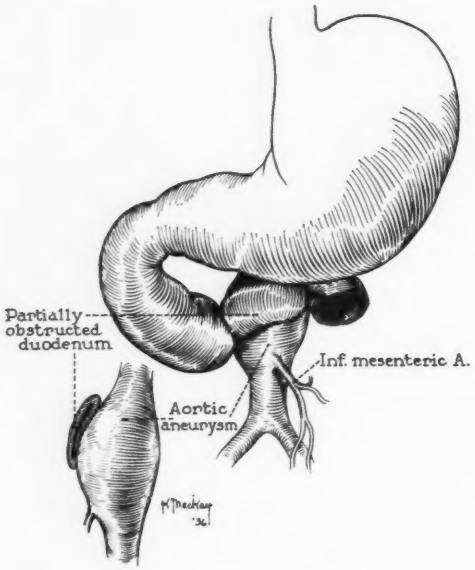

Fig. 2. Illustrating the relation of the aneurysm to the duodenum as seen at operation.

The symptoms caused by obstruction of the third portion of the duodenum resemble those of pyloric obstruction.

The case herein reported is one of obstruction of the third portion of the duodenum of extraduodenal nature, produced by pressure of an aneurysm of the abdominal aorta.

REPORT OF CASE

The patient, a white woman, aged 67 years, was admitted to the Clinic on Nov. 6, 1935, complaining of nausea and vomiting of two months' duration and of loss of weight. Approximately three years previously she had first begun to have symptoms of indigestion which lasted about ten weeks. During this time she had vomited almost constantly, regardless of whether she ate or not. Once during an attack she had vomited blood. These symptoms had then gradually disappeared without any particular treatment, and the patient regained her weight and strength. About two months before her admission, the previous symptoms recurred and then gradually progressed to the point where she could retain nothing on her stomach. A month later she noticed a mass in her abdomen which she thought had gradually increased in size.

On physical examination at the Clinic, the patient appeared to be well developed, but poorly nourished, weak, and obviously ill. The lungs were normal, the cardiac borders were within normal limits, and the heart beats were regular and clear. There was a palpable mass over which a faint bruit was audible, in the upper part of the abdomen, with visible, but not expansile, pulsation. The laboratory findings were as follows: urine, normal; hemoglobin, 15.9 gm. per 100 c.c.; leukocytes, 8,900 per cubic millimeter; flocculation test, negative, and total gastric acids 32 and free hydrochloric acid 16 units (Topfer's method). One hour after an Ewald test meal, 150 c.c. of gastric content was aspirated; this did not contain remnants of food but did contain a slight trace of blood. Occult blood was present in the stools.

On Nov. 15, 1935, roentgenoscopic examination of the stomach disclosed rather marked dilatation of the second portion of the duodenum and some stasis. There was a defect in the third portion of the duodenum indicative of an extrinsic lesion causing obstruction by pressure. As a pulsating abdominal mass was present in this region, it was surmised that the obstruction was caused by an aneurysm of the abdominal aorta. The clinical diagnosis was obstruction of the third portion of the duodenum, either by a dilated, tortuous aorta, or by an abdominal aortic aneurysm of diffuse type (Fig. 1).

On Nov. 22, 1935, the patient was operated on to relieve the obstruction. The stomach and duodenum were carefully examined but no evidence of an inflammatory lesion was found. There was, however, hypertrophy and dilatation of the duodenal wall, the result of an obstruction by an aneurysm of the abdominal aorta which measured approximately seven and one-half inches (19 cm.) in diameter (Fig. 2), for relief of which a posterior gastro-enterostomy was performed.

Obstruction of the third portion of the duodenum alone is a rather uncommon finding, and aneurysms of the abdominal aorta are likewise rare, particularly in that portion where the duodenum crosses the aorta. Rarer still, therefore, is obstruction of the third portion of the duodenum produced by an abdominal aneurysm.

OSTEOCHONDRITIS DISSECANS OF THE CAPITELLUM OF THE HUMERUS

By LEO FREDERICK MILLER, M.D., *Chicago*

From the service of Dr. H. B. Thomas, Orthopedic Department of the University of Illinois

Osteochondritis dissecans of the capitellum of the humerus is relatively rare, and only scattered reports are seen in the literature. This case is reported because it tends to further the explanation of the production of osteochondritis dissecans. Of those cases seen, the usual pathology of a dissecting fragment is already present and the diagnosis is quite obvious. It has been the writer's good fortune to observe this case over a period of months, with repeated roentgenograms taken at different intervals showing the development of the lesion.

The hypothesis as to the production of osteochondritis dissecans has been one of controversy since Monro advanced the theory of trauma as the basic cause for foreign bodies in joints. The literature can be divided into two groups as to the mode of production of the lesion: that in which trauma is the principal factor, and those factors other than trauma. It would be *apropos* at this time briefly to summarize the varied hypotheses.

The Theory of Traumatic Origin.—This may be sub-divided into: (*a*) subchondral fracture, (*b*) traumatic occlusion of the so-called end arteries of bone with the secondary involvement of the bone, (*c*) trauma resulting in inflammation of bone, or (*d*) superimposed injury on an already diseased bone.

The Theory of Nontraumatic Origin—This is (*a*) based on vascular involvement, (*b*) the result of inflammation, (*c*) heredity, or (*d*) chronic arthritis.

The study of the roentgenograms, or when the boy first appeared at the out-patient department, revealed a marked fragmentation of the capitellum of the humerus, and a definite zone of demarcation was present. The articulating surface was irregular and broken. After immobilization in a posterior molded cast, another film was taken one month later. The articulating surface had become more regular, and the fragments—which were three in the first film—now appeared as one. There was also a definite zone of absorption surrounding the fragment. The third roentgenogram, taken about one and a half months later, showed the presence of a cyst-like area with no fragmentation visible. Crossing this area of rarefaction were bone trabeculæ of a much coarser density. This rarefaction, however, was not so marked as it had appeared in the first roentgenograms. The fourth x-ray film was taken approximately six months after the boy appeared at the out-patient department of the orthopedic clinic.

Fig. 1. Showing the fragmentation of the capitellum, with the articulating surface irregular and broken and the presence of a zone of rarefaction. Film taken on June 20, 1935.

It is felt that the osteochondritis dissecans can be explained on the basis of the history of trauma, which was slight but repeated in character. This trauma was produced by the action of the head of the radius upon the capitellum of the humerus, with the result that the so-called end arteries were injured and a necrosis was produced. Axhausen says, in his description of the mode of production of osteochondritis, "As the result of impaction of opposing articular surfaces, the blood vessels to the part are damaged, either with or without partial fracture, according to the severity of the violence. This leads to necrosis of the area supplied by the damaged vessels. Instead of a creeping substitution of the necrotic

and overlying cartilage as would result in a case of aseptic necrosis in other regions, there forms a zone of absorption resulting in a gradual separation and eventually an extrusion

Fig. 2. Fig. 3.

Fig. 2. The fragmentation disappearing and a very definite zone of demarcation. Film taken on August 27, 1935.

Fig. 3. Showing the presence of a cyst-like area. Film taken on Oct. 4, 1935.

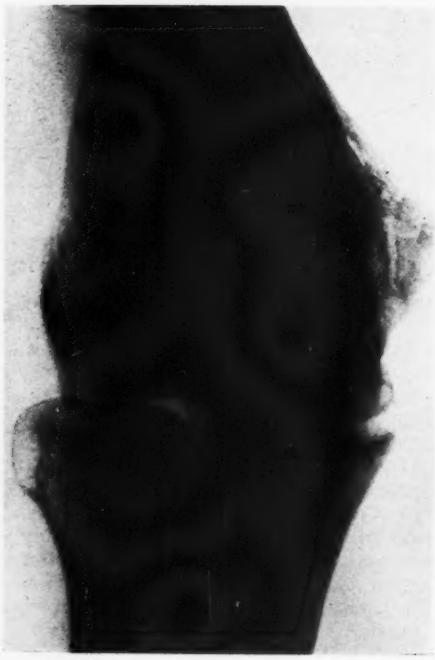

Fig. 4. Showing the typical picture of osteochondritis dissecans. Film taken on Dec. 6, 1935.

of the dead portion of bone into the joint." Axhausen's theory can readily be applied in this case, as seen in the serial roentgenograms.

REPORT OF CASE

History.—H. L., a white boy, 15 years of age, entered the orthopedic dispensary of the University of Illinois on June 14, 1935. The patient complained of a limitation of movement of the right elbow joint which, when in motion, was painful. There was a slight swelling as compared to the left joint. These symptoms had been present for the past month. He stated that he had never been troubled with the joint before the onset of pain. The patient attributed the onset to throwing newspapers daily while working on his newspaper route. The pain and limitation becoming gradually worse, the patient came to the clinic for treatment.

Physical examination revealed a tall boy, proportionally developed, with no evidence of endocrine disturbance. The essential findings were in the right elbow joint, where there was a localized puffiness just lateral to the olecranon process, with the skin of normal color. The lateral condyle was painful to slight pressure but no localized point of tenderness was present. Active motion revealed that the pain was most

marked in a combination of rotation and extension movement of the elbow joint. There was a loss of from 20 to 25 degrees of extension, and passive extension was not possible because of pain. The range of flexion and rotation was normal.

Treatment.—This consisted of the application of a posterior molded cast, and baking to the right elbow joint. The boy was kept under observation, and, at present, he has a loss of only five degrees of the carrying angle of the right elbow joint and is free of pain.

SUMMARY

A case of osteochondritis dissecans of the capitellum of the humerus is reported. The theory of the mode of production is based on the hypothesis of Axhausen.

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(2) AXHAUSEN: Die Entstehung der freien Gelenkkorper und ihre Beziehungen zur Arthritis deformans. Arch. f. klin. Chir., 1914, **104**, 581.

RADIOGRAPHIC TECHNIC FOR ACROMIOCLAVICULAR DISLOCATION[1]

By GERTRUDE R. PEARSON, R.T., Greeley Hospital, *Greeley, Colorado*

A review of the available literature does not teach us a method of roentgen examination which consistently shows acromioclavicular dislocation. The purpose of this paper is to pass on to others a radiographic method which, we have learned, reveals this injury in most cases. Routine shoulder radiography does not exclude acromioclavicular dislocation, even when the findings are apparently those of a normal shoulder.

Physicians tell us that acromioclavicular separation is ordinarily the result of direct force. When diagnosis and specific treatment are not accomplished early the patient is usually subject to "drop shoulder," which may hinder his daily activities.

If the superior and inferior acromioclavicular ligaments are injured, they go on to say, the major attachments of the acromion process and clavicle are severed. When the patient with an acromioclavicular dislocation is standing, the scapula sags slightly, separating the distal end of the clavicle from the acromion. If the patient is supine, the scapula is pushed upward so that, usually, the parts assume their normal relationship.

As an x-ray technician, I have x-rayed several cases which, the radiologist stated, showed separation plainly in the radiograph made when the patient was in the erect posture, but which presented normal acromioclavicular relationship in those plates made in the usual recumbent posture.

Figures 1 and 2 are reproductions of one of the cases. Note that the joint relations appear normal in the routine plates and severe acromioclavicular dislocation is recorded in those made on the same patient in the erect posture.

[1] Submitted through the advice of K. D. A. Allen, M.D.

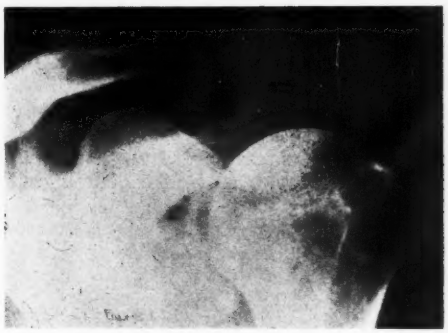

Fig. 1. Radiograph of a shoulder made in the routine supine position, showing normal appearance of acromioclavicular joint.

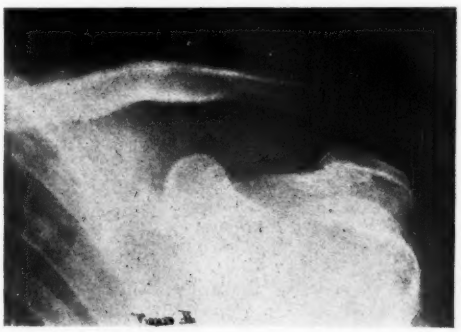

Fig. 2. Radiograph of the same patient as illustrated in Figure 1, made in the erect posture, showing acromioclavicular dislocation.

SUMMARY

1. Acromioclavicular dislocation is often overlooked clinically and is usually not shown on the routine anteroposterior films.

2. A series of cases reveals to the radiologist that acromioclavicular dislocation is demonstrated on films made in the erect posture.

Child Research Council,
4200 East Ninth Ave.,
Denver, Colorado

LATERAL ROENTGEN-RAY STUDY OF THE HIP JOINT[1]

By LEWIS J. FRIEDMAN, M.D., *New York City*

There have been many methods described during the past few years, each tending to simplify the lateral projection of the hip joint. The author wishes to present still another method which, in his experience, has proven to be simplicity itself.

There is no need for any unusual devices, since the standard Bucky table, cassette, and tube stand are employed. The position of the patient and the proper angulation of the roentgen-ray tube are the only requisites necessary for assuring proper technic.

Figure 1 depicts a pelvis and both femora placed almost laterally but with a 10° backward inclination of the normal side; the cone is inclined upward about 35°. In this position, the projected central rays are directed anteriorly to the normal femur and through the inferior surface of the femoral cervix under study.

The resulting radiograph (Fig. 3) reveals slight elongation of the femoral neck and exaggeration of the fracture which is actually present in this patient. In more extensive fractures, the position of the neck in relation to the trochanters may also be vividly seen. In the conventional study of the hip joint, one can occasionally notice only extremely vague evidences of fracture, as shown in Figure 2, a radiograph taken of the same patient as Figure 3.

Should the patient have difficulty in assum-

[1] Accepted for publication Dec. 13, 1935.

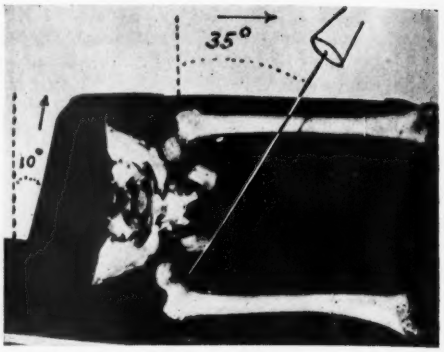

Fig. 1. The pelvis and both femora are placed almost laterally, but with a 10° backward inclination of the normal side; the cone is inclined upward about 35°.

Fig. 2.

Fig. 3.

Fig. 2. Conventional study of the hip joint, showing only extremely vague evidences of fracture.
Fig. 3. When the patient is placed in the position suggested by the author, the resulting radiograph reveals slight elongation of the femoral neck and exaggeration of the fracture which is actually present.

ing the posture described above, the roentgenogram may be made with the subject in the supine position. The tube is obviously placed on the side, and the suspected hip elevated to make up for the required 10° backward inclination.

SOLITARY OSTEITIS FIBROSA CYSTICA, COMPLICATED BY PATHOLOGIC FRACTURE AND TREATED LOCALLY BY ROENTGEN RAYS

By E. A. POHLE, M.D., PH.D., *and* L. W. PAUL, M.D., *Madison, Wisconsin*

From the Department of Radiology and Physical Therapy, University of Wisconsin Medical School

Osteitis fibrosa cystica in children is amenable to roentgen therapy; one must remember, however, that only moderate doses are indicated. If a pathologic fracture occurs in such an affected bone, it may heal satisfactorily following simple fixation (Geschickter). However, irradiation may definitely improve the end-result and hasten calcification of the cystic area. A case of this type will be reported below.

D. R., x-ray No. 4,683, white female, aged 6 years, was admitted to the orthopedic service of the State of Wisconsin General Hospital on March 28, 1935. At the age of two, she had injured her right arm by falling from a chair. The arm hung limp at the side for several days but she then regained normal use of it. In February, 1934, after having fallen several times, an x-ray examination was reported as showing "infected" bone and an old fracture in good position. Three days before admission to this hospital she fell again and injured the arm. The referring physician examined the arm with x-rays and found a pathologic fracture. The past medical history, other than that referable to the arm, was essentially negative.

Physical examination showed a child with normal development and nourishment for her age. The only pertinent findings were in the right arm. The right shoulder was depressed and the axillary fold was broadened anteriorly.

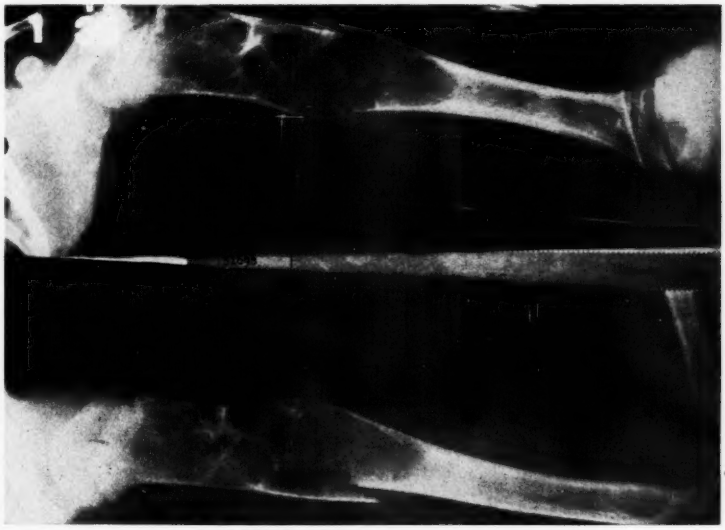

Fig. 1. Roentgenogram, taken on April 1, 1935, shows a pathologic fracture of the right humerus near the middle. Multilocular cystic lesions involving the proximal half of the humerus may be seen. There were no changes in the epiphysis.

The right arm measured seven and one-fourth inches in its greatest diameter as compared to six inches for the left. There was inability to abduct the shoulder or flex the forearm, and palpable crepitation and motion at the junction of the upper and middle thirds. A roentgenogram of the right humerus (Fig. 1) showed a pathologic fracture near the middle and osteitis cystica involving the proximal half of the humerus. No other bones were affected. Routine blood studies revealed a mild secondary anemia. The urine showed a trace of albumin on two occasions. The blood Wassermann was

negative. On July 17, the blood calcium was 10.3 mg. per 100 c.c., while the blood phosphorus was 4.4 mg. (normal values: 10–12 mg., and 4–5 mg., respectively). Until April 29, 1935, orthopedic treatment consisted of adhesive traction. The fracture had healed (Fig. 2) and the patient was referred to us for irradiation of the cystic lesions.

Fig. 2. Roentgenogram taken on April 29, 1935, after the removal of traction and before the starting of x-ray therapy. There is union of the fracture with callus formation; expansion of the shaft persists.

Fig. 3. Roentgenogram taken on July 8, 1935, shows the fracture healed in good position. There is a beginning recalcification of the cysts.

Fig. 4. Roentgenogram taken on Feb. 3, 1936, shows further calcification of the upper humerus, with reduction in diameter of the involved bone.

A total of three series of treatments directed to the anterior aspect of the upper right humerus was given in May, July, and October, 1935. Each series consisted of three sittings on alternating days; the dose amounted to 150 r (in air); half value layer in copper = 0.8 mm. Recalcification was noted in July (Fig. 3), and a more recent examination on Feb. 3, 1936, showed further calcification and reduction of the diameter of the involved bone (Fig. 4).

The question arises, of course, whether or not the healing fracture alone with its accompanying shift of calcium would have brought about this end-result. We feel, however, that x-ray therapy was of definite benefit particularly because of the continued calcium deposit after the fracture itself had healed (compare Figs. 3 and 4). The decrease in the size of the cysts was most marked during the period from July, 1935, *i.e.*, two and one-half months after healing of the fracture (Figs. 2, 3, and 4) to the date of the last examination. The probability of a spontaneous healing cannot be ruled out entirely.

EDITORIAL

LEON J. MENVILLE, M.D., *Editor* HOWARD P. DOUB, M.D., *Associate Editor*

WHITHER RADIOLOGY?[1]

Two radiologists, one a veteran and the other of the younger generation, delivered presidential addresses last week—Dr. L. A. Rowden, of Leeds, from the chair of the British Institute of Radiology, and Dr. C. G. Teall, of Birmingham, from that of the Section of Radiology of the Royal Society of Medicine. Dr. Rowden's address was an interesting excursion into the past. Just as there is a generation growing up to whom the war is only a tale told them by their fathers, so there are radiologists who have had no experience of inadequate apparatus or makeshift provisions, although the history of x-rays is comprehended within less than forty years. Dr. Rowden described the old tubes, coils, and mercury breaks, also the early measures for protection, which were not so inefficient as some people think. Dr. Teall, on the other hand, looked forward, counting himself fortunate to belong to a generation of radiologists who had known nothing but good apparatus of increasing facility. There was, however, one bogy about apparatus he wanted to lay. It was often asserted that with the advent of the push-button type of equipment almost everyone would be able to produce satisfactory radiographs. Unless the radiologist had the necessary knowledge of anatomy his beautiful picture might be quite useless, and the idea should be discouraged that radiographic technic was now quite easy. Dr. Teall went on to point out that with each fresh advance radiology was becoming more highly specialized. Two classes of radiologists were being developed: one the skilled consultant, the other the general practitioner of radiology. Advance would largely be made by the men who had taken a special interest in one branch of their work. On the other hand, while radiology became every year more specialized and difficult, comparatively cheap apparatus was also available. In the large towns a good radiological service in which the best type of apparatus was employed was usually provided, but the position was different in out-of-the-way districts, and this simpler apparatus enabled the country practitioner to make use of x-rays in his practice. The right policy was not to try to stop the use of such apparatus, but to ensure that practioners who employed it were instructed in its legitimate application and limitations. If only medical students were given an adequate knowledge of radiology in their curriculum, any danger from the more general employment of small apparatus would not be apprehended. Practitioners varied very much in the use that they made of the x-ray method. Some resorted to it infrequently, and their patients suffered in consequence; others relied too much upon it, and again their patients suffered. Dr. Teall desired to see the medical profession more radiologically minded, in the true sense of the word. The hospitals were now equipped with departments capable of all types of x-ray work, and the cost of such departments, both capital and maintenance, was very high. At the same time, many hospitals were adding private beds, and to the patients in such beds the facilities of these well-equipped departments would be available. The private radiologist could not compete with the service thus provided, and the radiologist, like the physician and surgeon, would do more and more of his work in institutions.

In conclusion, Dr. Teall referred to the Cambridge diploma in radiology. This and other diplomas since inaugurated had become not only recognized but regarded as an essential qualification for anyone who proposed to take up radiology. He wished it could be made one of the requirements for obtaining the diploma that candidates should have held at least one medical or surgical resident appointment. Many radiologists now took the view that a higher qualification still was necessary if the standard of radiology was to be maintained at a sufficiently high level to keep pace with developments in therapeutics and in diagnostic work. It might then be possible

[1] Reprinted by permission from British Med. Jour., Oct. 26, 1935.

to develop a college of radiology in which all the developments of radiological work would be fostered and co-ordinated. He believed that must be the ultimate goal.

NOTE BY THE EDITOR OF "RADIOLOGY"

Such a College of Radiology as Dr. Teall has envisaged has been established in North America, and now has an honorable record of several years' achievement and a membership composed of the most outstanding radiologists in the country.

COMMUNICATION

THE INDIANA ROENTGEN SOCIETY

The ninth annual meeting of the Indiana Roentgen Society was held in Indianapolis on June 7, this year. Dr. John D. Camp, of Rochester, Minn., addressed the society. His subject was "X-ray Findings in Spinal Cord Tumors."

The following officers were elected for the coming year: *President*, E. M. Van Buskirk, M.D., of Fort Wayne; *President-elect*, James N. Collins, M.D., of Indianapolis; *Vice-president*, H. H. Inlow, M.D., of Shelbyville; *Secretary-Treasurer*, Clifford C. Taylor, M.D., of Indianapolis.

ANNOUNCEMENTS

AMERICAN RADIUM SOCIETY

The next meeting of the American Radium Society will be held in Atlantic City, the Monday and Tuesday during the meeting of the American Medical Association, in the Spring of 1937.

The officers are:

President, Zoe Allison Johnston, M.D., Pittsburgh
President-elect, Edward H. Skinner, M.D. Kansas City
First Vice-President, Charles L. Martin, M.D., Dallas, Texas
Second vice-president, O. N. Meland, M.D., Los Angeles, Calif.
Treasurer, Lawrence Pomeroy, M.D., Cleveland, Ohio
Secretary, William P. Healy, M.D., New York City

BIOLOGICAL PHOTOGRAPHIC ASSOCIATION

The Biological Photographic Association extends a cordial invitation to all photographers and scientists interested, to visit its Sixth Annual Convention in Boston, Sept. 24–26, at the Hotel Lenox. Among others, the following papers will be presented:

Ultra-slow Mercuric "Spark" Motion Picture Apparatus, Dr. E. H. Edgerton, Massachusetts Institute of Technology.
Print Quality, Ralph P. Creer, Veterans Administration, Hines, Ill.
Infra-red Photography, Leo C. Massopust, Research Laboratory, School of Medicine, Marquette University, Milwaukee, Wis.
A paper on Otpics (title to be announced), Professor A. C. Hardy, Massachusetts Institute of Technology.
Ortho-stereoscopic Photography, Mr. Henry F. Kurtz, Scientific Bureau, Bausch & Lomb Optical Company.
Motion Pictures as an Aid in Teaching Entomology, Dr. C. T. Brues, Department of Biology, Harvard University, Cambridge, Mass.
Experimental Motion Pictures of the Larynx, Leonard Julin, Mayo Clinic, Rochester, Minn.

The exhibition will consist of photographs from all over the country and the most modern equipment and supplies.

The Association publishes a quarterly journal. It circulates its print exhibition as a travelling salon. It has a series of instructive illustrated loan albums for the use of its members.

Active membership is open to those whose duties include biological photography. Any one who is interested in such photography may become an associate member. The annual dues, including journal subscription, are $3.00.

Address the Secretary, Miss Anne Shiras, Magee Hospital, University of Pittsburgh, Pittsburgh, Pa.

Many members of the Radiological Society of North America will be interested in the activities of this Association because of a common interest in many phases of scientific photography.

NOTICE OF CORRECTION

In the paper by W. S. Middleton, O. O. Meyer, and E. A. Pohle entitled "The In-

fluence of Roentgen Therapy upon the Basal Metabolism in Leukemia," which appeared in the May issue, 1936, **26**, 586–594. Charts I and II should be reversed. The legends are correct as appearing in the paper. The authors overlooked the matter in their proof.

BOOK REVIEW

"MEDICAL PAPERS," dedicated to Henry Asbury Christian from his present and past associates and house officers of the Peter Bent Brigham Hospital, Boston, Massachusetts, in honor of his sixtieth birthday. Edited by ROBERT T. MONROE, M.D., Peter Bent Brigham Hospital. A volume of 1000 pages. Published by William Wood & Company (Waverly Press, Inc., Baltimore, Maryland, 1936). Price, $10.00.

This book in honor of Dr. Christian's sixtieth birthday contains over one hundred medical articles, each written expressly for the volume by Dr. Christian's present and past associates and house officers at the Peter Bent Brigham Hospital. The list of contributors contains the names of a remarkable number of men who are prominent to-day in American medicine, and serves to emphasize the great and widespread influence that Christian has had on medical thought in this country.

The subjects presented vary widely. Case reports, of which there are several, show the results of Christian's influence in the meticulous care with which the cases have been studied and the observations set down. The subject matter of the book is, in general, excellent. Aside from a few papers of a general nature, there are papers on circulatory disorders, renal diseases and diuretics, diseases of metabolism and the ductless glands, pulmonary diseases, diseases of the blood and liver, studies of the function of the intestines, studies of several infectious and parasitic diseases, and a group of miscellaneous papers. An excellent sketch of Christian's scientific life is given. The book is closed with a register of former and present members of the Peter Bent Brigham Hospital medical staff.

The volume presents an excellent cross-section of present-day medicine, and contains more authoritative and valuable information. It is to be regretted that there is no index. As a tribute to Dr. Christian, the book serves its purpose fittingly and admirably. It will, of course, be of particular value to the many distinguished members of the staff, both past and present, of the Peter Bent Brigham Hospital and to the hosts of friends and students of Dr. Christian.

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ABSCESS, PULMONARY

Serial Bronchography in the Diagnosis of Suppurative Pulmonary Processes. Pedro L. Fariñas. Am. Jour. Roentgenol. and Rad. Ther., November, 1935, **34**, 579–591.

For two years the writer has been studying cases of pulmonary abscess in various stages of development by the use of serial roentgenograms made under roentgenoscopic control after the injection of lipiodol through a catheter previously introduced through the nasal fossa and larynx into the main stem bronchus on the side of disease.

In the very earliest stages of development of an acute abscess there are no characteristic abnormalities of the bronchogram for, in this stage, the bronchial walls have not suffered the effects of the inflammatory process long enough to lose their elasticity and dilate. The iodized oil will not penetrate the alveoli which are filled with purulent exudate, hence the bronchographic appearance is that of a tree without leaves. Somewhat later, even after the formation of the cavity has progressed farther, it may be so full of secretion and the bronchial communication so inadequate that the oil will still fail to penetrate except where there is communication with the large bronchus, in which case the cavity proper may be demonstrated in the roentgenogram. Later, after the pneumonic process has resolved, the alveolar dispersion of the oil can be noted and the appearance of the bronchial tree is that of a tree with its leaves. At times, after the cavity has been draining for a while, there may be a cylindrical or ampullar dilatation of the bronchus draining the cavity, while the rest of the bronchial tree remains normal. There is another type of case, especially in post-operative abscess, in which there may be very early manifestations of cylindrical dilatation of the affected bronchi. In these cases the oil may not penetrate beyond the dilated medium-size bronchi, and in this event the appearance is that of a dead tree. Sometimes when a bronchopneumonic process becomes suppurative the oil filling will demonstrate numerous small abscesses separate one from another.

In the chronic cavity formation there is usually ample bronchial communication and the filling of the cavity proper is readily accomplished. Very commonly, even when the draining bronchus presents a relatively normal appearance, the bronchi toward the base of the lung on the same side will show cylindrical and sacciform dilatation. These changes in the basal bronchi are believed to be due to the constant tendency toward drainage of purulent bronchial secretion into this part of the tree.

Sometimes the differentiation between bronchiectatic abscess and abscessed bronchiectasis may be difficult; in the former condition there is apt to be a larger central cavity, with smaller sacciform cavities around it, while in the latter condition of abscessed bronchiectasis all of the cavities are of about the same size.

In ulcerating bronchial carcinoma a filling of the cavity with oil may occur, but one will not find sacciform dilatations of the bronchi about this area.

In ulcerating lobar carcinoma, the cavity generally does not fill and the whole bronchial tree at this level is displaced by the tumor. J. E. Habbe, M.D.

ANIMAL EXPERIMENTATION

Production of Sarcoma by Colloidal Thorium Dioxide in the White Rat. G. Roussy, Ch. Oberling, and M. Guerin. Strahlentherapie, 1936, **56**, 160.

When studying the effect of colloidal thorium dioxide on transplanted tumors of the white rat the authors noted the appearance of a peritoneal sarcomatosis one year after thorotrast injections. This induced them to study the possibility of further producing sarcoma by injections of thorotrast. In rats, mice, and chickens it was possible to produce sarcomatous neoplasms which were eventually fatal to the carrier. A series of photomicrograms are appended showing the histologic structure of the tumors.

While there may be no danger of development of sarcoma in patients who receive thorotrast injections for diagnostic purposes, the authors feel that caution is indicated when using even slightly radio-active substances.

Ernst A. Pohle, M.D., Ph.D.

Observations of Cell Changes during Roentgen Irradiation. J. Heeren. Strahlentherapie, 1936, **55**, 263.

The author studied the effect of roentgen rays on frog muscles and on liver cells during irradiation. The technic is described in detail. The frog muscle contracts during irradiation. Whether or not a second exposure produces the same phenomenon depends on the condition of the muscle and also on the time interval between the two exposures. The magnitude of the dose has undoubtedly also some influence on the reaction. The metabolism of liver tissue is definitely decreased during irradiation, provided that the cells are exposed in Ringer's solution. If serum is used, there is hardly any change in the metabolism to be detected. Further investigations regarding qualitative changes in the irradiated cells are promised.

Ernst A. Pohle, M.D., Ph.D.

Radiobiologic Studies on the Skin of the Himalaja Rabbit. O. Becker. Strahlentherapie, 1936, **55**, 316.

The author compared the effect of Grenz rays (9 kv.) and roentgen rays of moderate penetration (150 kv., 3 mm. Al). It appeared that neither erythema nor pigmentation constituted suitable reactions for such a study. However, the desquamation in the skin could be used. It occurred after 650 r of Grenz rays and 750 r of roentgen rays of the quality described above. There was no difference in the cumulation of the dose between Grenz rays and roentgen rays.

Ernst A. Pohle, M.D., Ph.D.

X-ray Diffraction Patterns from Reprecipitated Connective Tissue. Ralph W. G. Wyckoff and Robert B. Corey. Proc. Soc. Exp. Biol. and Med., March, 1936, **34**, 285–287.

A series of experiments was carried out to determine: (*a*) whether reprecipitated tendon is really crystalline, and (*b*) whether its x-ray diffraction pattern is like that of the original tissue.

Using acid solutions of tail tendon from adult rats, x-ray diffraction studies have been made. Diffraction patterns were photographed and measured from (1) the original tail tendon after drying over P_2O_5, (2) reprecipitated tissue dried under tension, (3) the extracted tendon dried under tension. Results prove that reprecipitated tissue shows exactly the same x-ray diffraction lines as the original tendon. Such a reprecipitated tissue can differ only slightly if at all from the original either in chemical composition or in crystalline array. Since such collagen solutions may be expected to contain substantially the same large molecules that have gone to make up the original connective tissue, a study of such solutions can hardly fail to throw light upon the nature of these molecules.

W. A. Sodeman, M.D.

The Behavior of Reticulocytes of the White Mouse Following Roentgen Irradiation. H. Langendorff. Strahlentherapie, 1936, **55**, 307.

In this first paper the author studied the effect of a single dose of roentgen rays on the reticulocytes of the white mouse. The animals were kept one week under the same conditions and then exposed to 180 kv., 3 mm. Al for from one to 18 minutes, corresponding to from 50 to 800 r. The animals tolerated this dose fairly well except that two mice exposed to 800 r died. The normal value for reticulocytes in the white mouse was determined in 118 animals; it amounted to 89.6 o/oo. The count was taken daily following irradiation and the results were plotted. The resulting curve corresponded to the erythema curve of the skin or to a mitosis curve determined following roentgen exposure. If the animals were anesthetized, the effect of irradiation was more pronounced. Various narcotics showed, however, a difference in this reaction. No permanent injuries of the reticulocytes could be observed even though the dose used approached the lethal dose.

Ernst A. Pohle, M.D., Ph.D.

APPARATUS

Continuously Evacuated X-ray Tubes. T. E. Allibone. Proc. Royal Soc. Med., March, 1936, **29**, 439–448.

Allibone reviews the development of the methods of evacuation of the x-ray tube to the use of the vapor condensation pump. C. R. Burch, of the Metropolitan-Vickers Electrical Company, while studying the oil impregnation of a number of insulating materials under vacuum, discovered that he could separate the light fractions of the oil from the heavy, thus collecting a fraction with very low vapor tension. This oil could be employed in a single-stage metal condensation pump which once used mercury to produce pressures far below that of "x-ray vacuum" without the necessity for a cooling reagent. He could produce pressures as low as 10^{-4} dynes/cm.^{2} at normal temperatures. Burch also discovered a number of low vapor tension viscous fluids which can be used for sealing joints and the like.

With the need for a refrigerant eliminated, it was possible to construct an x-ray tube of durability and with very low pressure by the use of continuous evacuation. Experimental x-ray tubes and rectifiers have been evacuated by these oil pumps and operated up to 350 kv. A tube for medical deep x-ray therapy has been constructed which is efficient, almost indestructible, and shockproof. This new tube can operate at any current up to 10 ma. and on a steady voltage of from 200 to 250 kv. The cathode and anticathode are so constructed that they can be replaced in a short time.

The tube, which is well illustrated and described by Allibone, is mounted so that it is easily manipulated and controlled. Many of the important features of this porcelain-and-steel-enclosed tube with a greater output than that customary for glass tubes are discussed.

These continuously evacuated tubes are being developed in many parts of the world where high voltage tubes are pumped with Apiezon oils and are operated with varying degrees of success.

George E. Burch, M.D.

Dosimetry with the Mecapion in Contact Roentgen Therapy. S. Strauss. Strahlentherapie, 1936, **55**, 537.

The author briefly describes a modification of the mecapion adapted especially for use in x-ray therapy at very small F.S.D., according to the method described by Chaoul.

Ernst A. Pohle, M.D., Ph.D.

A Simple Device for Remote Control of Filter and Shutter in Superficial Therapy. S. Epstein. Strahlentherapie, 1936, **55**, 366.

The author describes briefly a shutter attached to the x-ray tube which can be operated from the control booth. The operator can insert the proper filter or a lead shutter without leaving the control stand. A pilot light operating in connection with the device shows when the filter is in place.

Ernst A. Pohle, M.D., Ph.D.

Experiences in Manchester with the Metropolitan-Vickers Tube. Ralston Paterson. Proc. Royal Soc. Med., March, 1936, **29**, 449–452.

Paterson concludes from his experiences with the Metropolitan-Vickers tube that it is a satisfactory and reliable unit. The replacement and difficulties that were encountered were rapidly and easily cared for. The tube has a high initial cost but a low running cost. It is readily manipulated for extremely short or long exposures at varying intensities.

George E. Burch, M.D.

ARTERIOGRAPHY

Arteriography of the Brain. H. Urban. Wien. klin. Wchnschr., July 12, 1935, **48,** 924–927. (Reprinted by permission from British Med. Jour., Dec. 7, 1935, p. 89 of Epitome of Current Medical Literature.)

The author describes the use of thorotrast in this procedure. Under local anesthesia, 10 c.c. are injected into the commencement of the internal carotid artery as quickly as possible, and the x-ray film is taken just before completion of the injection (so quick is the circulation through the brain that a second later the thorotrast is traceable in the veins only). The medium is stored indefinitely in the liver and spleen. The arterial injection is painless, causes but a few seconds, stupor, and may lead to a transitory disappearance of headaches if present. Only the lateral radiograph is instructive; and in it the posterior cerebral artery (coming indirectly from the vertebral) is not shown. This artery can be traced by thorotrast injection of the subclavian, the artery being clamped distally and the syringe directed toward the heart: through the innominate artery the basilar artery and the posterior cerebral arteries of both sides are injected. For comparison in the ordinary procedure the lateral radiographs of both sides should be taken at the same sitting.

From an experience of 50 cases Urban concludes that while arteriography is of considerable help in localization of cerebral tumors, its chief value is in determining their nature—especially in angiomas, aneurysms, and arteriovenous communications behind the orbit.

ARTHRITIS

Roentgenographic Features of Rheumatoid Arthritis. Albert B. Ferguson. Jour. Bone and Joint Surg., April, 1936, **18,** 297–300.

Rheumatoid arthritis is defined as "that form of multiple arthritis which begins before the age of 35 years and tends to loss of cartilage and bone at the joints, deformity and eventual ankylosis, emaciation of the patient, elevation of the sedimentation rate of the blood, and positive response to the streptococcus agglutination test."

In the roentgen study of rheumatoid arthritis the hands, feet, knees, and lumbar spine should be examined in every case. The soft tissues should be clearly shown in all cases, as certain changes are noted in the soft tissues in the region of the joints and in the relative densities of soft tissues and bone.

In the early stages of rheumatoid arthritis the roentgen signs consist of a uniform decrease in density, particularly in the hands and feet, and the appearance of a fusiform soft tissue mass in the region of the joints, especially the phalangeal articulations. Later stages of the disease show by roentgen examination evidence of "punched-out" rounded areas of loss of bone at the junction of the cartilage and bone in the region of the joint. Other findings consist of thinning of the cartilaginous joint space, and ankylosis. With repair, calcareous lipping at the margin of the joint is noted.

Because of the great mass of tissue involved in rheumatoid arthritis in the spine, the slight changes found in other joints are not usually noted. However, the usual roentgen findings in this locality are slurring of the articular facets, irregular depressions in the articular surfaces of the facets, and ankylosis without loss of the intervertebral discs.

Rheumatoid arthritis must be differentiated from osteo-arthritis, gout, and specific infections of the joints. Atrophic arthritis of the toes following gonorrhea is believed to be a special type of rheumatoid arthritis.

J. N. Ané, M.D.

BIOLOGIC EFFECTS OF RADIATION

The Effect of X-rays on Cleavage in Arbacia Eggs: Evidence of Nuclear Control of Division Rate. P. S. Henshaw and D. S. Francis. Biol. Bull., February, 1936, **70,** 28–35.

Henshaw and Francis studied the effect of irradiation by the x-rays on the cleavage rate of the fertilized eggs of *Arbacia punctulata*. They divided their observations into four groups: normal eggs fertilized by normal sperm, irradiated eggs fertilized by normal sperm, normal eggs fertilized by irradiated sperm, and irradiated eggs fertilized by irradiated sperm. The first group was used as controls with which the results in the other three groups were compared. The authors found that in the last group the cleavage rate was delayed most, and delayed least in the second group. They conjectured as to the possible effect of irradiation on the gametes, the effect probably being greatest on the nuclear material and probably to some extent on the centrosomes. They claim priority for such observations and conclude that the method employed offers a quantitative estimate of radiobiological reactions.

George E. Burch, Jr., M.D.

BONE DISEASES (DIAGNOSIS)

Dystrophies of the Skeleton. J. F. Brailsford. British Jour. Radiol., September, 1935, **8,** 533–569. (Reprinted by permission from British Jour. Med., Dec. 7, 1935, p. 89 of Epitome of Current Medical Literature.)

The author has made a study of the serial radiographic appearances of the entire skeleton in cases of dystrophy, and as a result defines ten groups, namely, "marble bone disease" (Albers-Schönberg); osteogenesis imperfecta (Vrolik and Lobstein's types); ateleiotic midgets and infantilism (Lorain); achondroplasia (Parrot); chondro-osteo-dystrophy (Brailsford); multiple exostoses or diaphyseal actasis (Keith); multiple chondromas (Ollier); unclassified dystrophies, including such types as cranio-cleido-dysostosis, acrocephalosyndactylia, and arachnodactyly; dystrophies as-

sociated with endocrine disorders, and dystrophies associated with other diseases. All these have characteristic radiographic appearances.

Although it is not always possible to obtain evidence of hereditary influences, the indications are so definite in some cases that Brailsford thinks it necessary to consider the probability of there being a recessive factor concerned. None of these dystrophies has been found to possess characteristic histologic findings or specific biochemical reaction, and so far these dystrophies have not for the most part been related to endocrine dysfunction. No checking of their development has proved possible, except in the case of multiple exostoses and chondromas (which may be treated by local surgical excision), so it is in differential diagnosis that a knowledge of these surgical dystrophies is of most importance.

Paget's Disease (Osteitis Deformans). Alexander B. Gutman and Haig Kasabach. Am. Jour. Med. Sci., March, 1936, **191,** 361–380.

Gutman and Kasabach point out the importance of the roentgenographic examination in Paget's disease. Clinical evidence sufficient to warrant the diagnosis was absent in almost two-thirds of 104 cases. Radiologic study was considered essential for confirmation of the diagnosis as well as for determining the extent and character of the pathology in various bones.

In 14 cases the lesions appeared to be localized to a single area. Early lesions in long bones were confined often to one end of the shaft. In many of the early cases only one side of the pelvis was involved. Since osteitis deformans may become arrested at any stage, it would seem hazardous to draw from a single roentgenogram any conclusions as to the activity of bone changes or to predict the course of the disease.

Early skull changes were seen most frequently in the frontal and frontoparietal regions, rarely in the occipital regions alone. Involvement of the base of the skull was unusual. Generalized decalcification of the skeleton of the type seen in hyperparathyroidism was not encountered. Varying degrees of osteoporosis were seen associated with co-existing marked arthritis or in cases in which the patient was confined to bed as the result of fractures or deformities. Cyst-like changes were seen occasionally at the proximal ends of the femora or humeri. The bones most commonly involved were the pelvis, skull, femur, humerus, lumbosacral spine, and the tibia.

W. A. Sodeman, M.D.

Concerning the Genesis of "Madelung's Deformity." W. L. Beder and J. I. Heinismann. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1935, **52,** 595–601.

Two case reports are added to the existing literature on this subject. In addition to the deformities, both cases presented endocrine disturbances interpreted as hypophyseal eunochoidism. The authors want to separate true Magelung's deformity resulting from primary disturbance of bony growth and endocrine dysfunction from pseudo-Magelung's deformity induced by trauma, arthritis, osteomyelitis, etc.

H. A. Jarre, M.D.

Epicondylitis Humeri (Tennis Arm). Wilhelm Thomsen. München. med. Wchnschr., Nov. 8, 1935, **82,** 1804–1807.

The condition in the light of recent knowledge is unquestionably a myositis of chronic nature, with round-cell infiltration about nerve fibrils and vessels, and with contiguous periostitis in a percentage of cases. The latter incidence is indeterminate, and probably very often associated in marked cases, and contrariwise, in the less severe types. It follows that roentgenographic demonstration of periostitis will vary with the above conditions, and even when present will not be amenable to demonstration in the very early case. The entity is never a form of arthritis deformans or neuritis, according to the author.

Anatomic and operative studies disclose the extensor digitorum communis muscle to be mainly involved, at its site of insertion. Whether traction or adjacent myositis excites periosteal reaction is a moot question; probably both factors are involved. Curiously, it has been noted that the left arm in right-handed persons is frequently involved, which to some degree discredits the excessive trauma theory of etiology. Poor blood supply and fibrositis are strong contributory factors, the author noting this condition in a high percentage of individuals without symptoms. Therapy should be preventive, by massage prior to engaging in arduous exercise of certain muscle groups; *viz.*, in tennis. Conservative treatment consisting of absolute immobilization and heat are employed in the well-established case; whereas, massage and heat are efficacious in the very early and late stages of the affection.

William R. Stecher, M.D.

Some Notes on the Diagnosis of Bone Tumors. H. R. Sear. British Med. Jour., Jan. 11, 1936, No. 3,914, 49–53.

The author discusses the roentgen findings in the various classes of bone tumors. He is of the opinion that errors in diagnosis result from lack of care in interpretation, failure to make use of history and pathologic findings, and from lack of experience and knowledge.

The radiologist should have available complete clinical and pathologic laboratory findings. He should feel free to request further laboratory procedures and to make additional x-ray examination if necessary for differential diagnosis. Serial roentgenograms may be necessary to study the progress of a disease, although the procedure should be avoided if at all possible because of the greater danger to the patient occasioned by the delay.

For this discussion the bone tumors are classified as follows: (1) changes involving mainly the periosteum or the surface of the cortex; (2) cortical changes; (3) central lesions; (4) composite involvement.

The periosteal tumors included are: (1) secondaries from primary bronchiogenic carcinoma; (2) extraperiosteal fibrosarcoma; (3) secondary neuroblastoma; (4) specific periostitis.

Two types of hypertrophic pulmonary osteo-arthro-

pathy have been recognized. One type is the true osteo-arthropathy seen in bronchiectasis, etc., and the other type, which is seen in bronchiogenic carcinoma. There is also single bone metastasis found in this condition. This is noted at roentgen examination as a localized lesion, with slight to moderate cortical erosion, and with definite periosteal reaction arranged in a loculated manner. It is not unlike the soap-bubble appearance seen at times in secondary hypernephroma.

Extra-periosteal fibrosarcoma is the most benign of all sarcomas, and local removal is considered sufficient for its cure. It is characterized by a pressure deformity on the adjacent bone, without erosion.

Secondary neuroblastoma is seen in infancy and the early case is characterized by slight elevation of the periosteum sometimes associated with lipping. The skull and long bones are affected. The history reveals inability of the child to use its legs and the blood count shows a marked decrease in red cells.

Syphilitic bone disease may assume many forms, such as osteosclerosis or primary cortical involvement. However, the peculiar "lace-work" type of periostitis also may be noted.

The cortical tumors discussed by the author are: (1) hydatid; (2) lymphadenoma; (3) secondary involvements, such as hypernephroma.

Hydatid disease in bone is comparatively common in Australia (the author's home) and is noted as the central or cortical type of lesion. The cortical type presents erosion with more or less bone production. Of great value in the differential diagnosis is the eosinophilia and the Casoni test.

Lymphadenoma is seen most frequently in the sternum. It may occur also in the vertebræ, pelvis, skull, ribs, and femora. It is characterized by bone erosion and bone production in variable proportions. Of diagnostic importance is its ready response to irradiation therapy.

Secondary or metastatic tumors frequently involve a single bone and may prove difficult to differentiate from osteogenic sarcoma of the osteolytic type. The bone metastasis of hypernephroma may be of the central or cortical types. The cortical type is usually seen in the flat bones. The appearance of such lesions has been likened to "soap bubbles."

The central lesions considered are: (1) the central type of hydatid; (2) lipoid histiocytosis; (3) central cartilaginous masses and tumors, and (4) metastatic hypernephroma.

The central type of hydatid extends up and down the medullary cavity and simulates bone cyst. The differentiation is difficult in some cases and pathologic assistance must be obtained.

Lipoid histiocytosis has been described by Schüller as the geographical skull and by Gaucher as affecting the long bones. Schüller's and Gaucher's diseases may be seen at times in the same individual.

Central cartilaginous masses and tumors include chondrosarcoma and myxochondrosarcoma, which may simulate cystic lesions in bone.

The composite tumors include Ewing's tumor, Paget's disease, lipoid histiocytosis, and secondary neuroblastoma.

Ewing's tumor may prove extremely difficult to recognize in some cases. It is frequently confused with osteomyelitis. Early cases of Ewing's show increased density in the affected area. It may have an acute onset with fever, pain, and leukocytosis.

Paget's disease or osteitis deformans must be differentiated from secondaries of prostatic carcinoma. Of greater difficulty, however, is the recognition of early sarcoma when it supervenes on a bone affected with Paget's disease.

Gaucher's disease causes thinning of the cortex and a worm-eaten appearance of the long bones. The differential diagnosis must be made from tuberculosis of bones.

Secondary neuroblastomas are usually characterized by the worm-eaten appearance of the long bones and the periosteal reaction, with, later, the formation of larger transradiant areas.

J. N. Ané, M.D.

THE BRAIN

Review, Clinical and Pathological, of Parahypophyseal Lesions. C. H. Frazier. Surg., Gynec. and Obst., January, 1936, **62,** 1; February, 1936, **62,** 158. (Reprinted by permission from British Med. Jour., March 14, 1936, p. 44 of Epitome of Current Medical Literature.)

The author records a clinical and pathological review of various parahypophyseal lesions, and comments on the extraordinary advances in the surgery of brain tumors during the last forty years. The lesions are classified in eight groups. The first of these includes parasellar aneurysms, which are sometimes of congenital origin and sometimes due to arteriosclerosis. Mycotic aneurysms are more common in the cerebral than in the basilar vessels. Two cases are reported in which there were intense headaches and periods of momentary unconsciousness. In both instances the patient died, and at necropsy an aneurysm was located. Tumors of the optic nerves and chiasm are comparatively rare, and can be diagnosed only as a result of specific x-ray findings. When the tumor is small there may be only optic atrophy, field defects, and loss of visual acuity. Later, headache may develop, with signs of hypophyseal dysfunction and characteristic alterations in the sella and optic foramina.

These tumors occur most frequently in children, and radical removal is inadvisable on account of the inevitable blindness that would result. The most common location for parasellar tumors is the sphenoidal ridge, and the most usual type of growth is the meningeal fibroblastoma. The most frequent symptoms are the loss of visual acuity, field distortions, and homonymous hemianopsia. A case is reported in which recovery followed the excision of the tumor. Surgical treatment in cases of suprasellar pseudo-tumors is most satisfactory. Diagnosis must depend on the visual phenomena, loss of visual acuity, field distortions, hemianop-

sia, or a concentric contraction of vision. Tumors of Rathke's cleft, hypophyseal stalk tumors, and suprasellar fibroblastomas are also described, with illustrative cases.

BREAST (BENIGN)

Roentgen Therapy of the Bleeding Breast. P. Gibert. Strahlentherapie, 1936, **56,** 81.

The author has observed in his practice eight cases of bleeding breast, which he treated with roentgen therapy. Technic: 120 kv., 10 mm. Al three areas over anteroposterior breast, axilla, and supraclavicular region, 16 × 16 cm. field size at 40 cm. F.S.D., 1,600 to 2,000 r in five sittings. One patient has been observed over a period of 11 years and has remained well. Before subjecting any patient to this therapy, malignancy must be definitely ruled out.

ERNST A. POHLE, M.D., Ph.D.

BREAST CANCER

Roentgen Therapy of Advanced Carcinoma of the Breast. H. Holfelder. Strahlentherapie, 1936, **56,** 97.

The author states that x-ray therapy in advanced carcinoma of the breast should be given a trial. He quotes four illustrative case reports, with photographs of the patient before and after treatment. Palliative results were very encouraging; as a matter of fact, in several instances the growth disappeared completely. Technic: 190 kv., H.V.L.$_{Cu}$ 1.0 mm., doses of from 6,000 to 10,000 r per series spread over periods of from four to eight weeks; simple fractional method with multiple fields.

ERNST A. POHLE, M.D., Ph.D.

The Effect of Ovarian Irradiation on the Bone Metastases of Cancer of the Breast. Richard Dresser. Am. Jour. Roentgenol. and Rad. Ther., March, 1936, **35,** 384–388.

In the 5-year interval between 1929 and 1934, 59 cases of cancer of the breast with bone metastases have received ovarian irradiation, 30 being women under 45, and 29 of post-menopausal age. Of the group of 30 below menopausal age, nine (or 30 per cent) showed definite regression of bone metastases. These results have encouraged the writer to extend ovarian irradiation to women under 45 years of age even when no bone metastases have developed. The author's technic is 200 kv., 0.5 mm. copper, 600 r measured in air, to one anterior pelvic field 15 × 15 cm., and one posterior pelvic field of the same size.

J. E. HABBE, M.D.

The Treatment of Inoperable, Recurrent, and Metastatic Carcinoma of the Breast. Eugene T. Leddy and Arthur U. Desjardins. Am. Jour. Roentgenol. and Rad. Ther., March, 1936, **35,** 371–383.

Inoperable carcinoma of the breast is best treated by roentgen therapy using multiple converging beams with a combination of buried radium in selected cases.

Operable recurrences are best treated by operation supplemented by roentgen therapy, the results of roentgen treatment being in every way equal to those obtained with radium. Local recurrence of carcinoma in the field of operation is the most favorable to treat, whereas axillary recurrence in general has the worst prognosis. The commonest type of metastases was to the supraclavicular nodes. Roentgen therapy is recommended but its value is difficult to state. Lung and liver metastases respond poorly but osseous metastases favorably.

There is little evidence of superiority of radium or 200 kv. roentgen therapy over 135 kv. x-rays; in fact, in some lesions the latter appears preferable.

J. E. HABBE, M.D.

Indications for Radical Surgery of the Breast. Hugh Auchincloss. Am. Jour. Roentgenol. and Rad. Ther., March, 1936, **35,** 344–347.

Radical surgery in malignant disease of the breast is contra-indicated in cases in which the disease has spread beyond the limits capable of being removed by operation. The young individual presenting a tumor with rapid growth, with already existing large hard axillary nodes, or a lesion already fixed to and involving the chest wall near the sternum, or one with much nipple involvement and widespread lymphedema, or one in which may dilated veins and beginning skin ulceration are evident—these and certain other combinations may lead one to infer that the case is not suitable for surgery. However, in the opinion of the author, unless the disease has spread beyond the point where it can be removed, the patient should be given the benefit of the doubt and operated upon. The author has seen many cases, considered clinically hopeless, which were so helped by irradiation that suffering was relieved and even subsequent operation done. Post-operative irradiation is of definite value.

In addition to the usual and perhaps most commonly encountered extension to the axillary glands, there are other routes which must also be continuously considered. There are lymph channels which go along the branches of the internal mammary arteries. The internal mammary nodes that communicate with the retro-manubrial nodes at the prepericardial nodes near the diaphragm receive much lymph from the breast. Again, lymph channels enter the space between external and internal intercostal muscles. These external intercostal lymph vessels run backward to enter the posterior intercostal lymph nodes in front of the necks of the ribs close to the spine. Still again, there are lymphatics communicating between the axilla, the skull, and the scalp which may account for the frequency of metastases in these last-named regions.

The author concludes with a plea for instruction of the laity as to the importance of the woman regularly examining herself for evidence of a "lump" in the breast. Then she may commonly be able to determine the presence of a pathological mass, after she has become skilled in self-examination, which the doctor may himself not be able to feel.

J. E. HABBE, M.D.

CANCER (DIAGNOSIS)

Malignant Tumors of the Epipharynx. S. Salinger and S. J. Pearlman. Arch. Otolaryngol., February, 1936, **23,** 149–172. (Reprinted by permission from British Med. Jour., May 16, 1936, p. 81 of Epitome of Current Medical Literature.)

In an attempt to clarify the nomenclature of malignant tumors of the nasopharynx the authors record a histopathological investigation of 24 cases. The commonest type in the opinion of three pathologists was transitional cell carcinoma (75 per cent). In three instances the diagnosis of sarcoma was considered, but was unanimously approved in only one. Lymphoepithelioma was diagnosed in six cases, and it was noted that the uncertainty as regards diagnosis was partly due to the similarity of this growth to transitional cell carcinoma and also to inadequate fixing and staining of the sections. Endothelioma was mentioned once by one pathologist, and contested by the two others.

The early and characteristic symptoms of transitional cell carcinoma were found to be: painless cervical adenopathy, tinnitus or deafness, and pains due to involvement of the first and second branches of the trifacial nerve. In most cases in this series the tumor was found to have originated in the region of the Eustachian tube of the lateral wall of the nasopharynx, thus accounting for the symptoms.

The authors agree that these tumors are not amenable to surgery. Treatment consists of external irradiation by means of x-rays or radium packs, associated in some cases with the surface application of radium to the growth. Adequate filtration is utilized to obtain the highest degree of penetration. The total dose is estimated biologically, the aim being to cause complete regression of the growth without permanent damage to the adjacent normal structures.

CANCER (THERAPY)

Development and Treatment of Cancer *en cuirasse*. H. T. Schreus. Strahlentherapie, 1936, **56,** 168.

The author states that most cases of cancer *en cuirasse* occur in patients following operation; it is very rarely observed in others. While this type of cancer is usually a most hopeless condition, radiation therapy should be given a trial. The following technic proved of value in the author's experience: 80–100 kv., no filter, 300 r per area, 15 × 15 cm. field size, total doses up to 3,600 r. While there are no 5-year statistics available, the preliminary results have been encouraging.

ERNST A. POHLE, M.D., Ph.D.

The Effect of Pre-operative Irradiation in Primary Operable Cancer of the Breast. Frank E. Adair. Am. Jour. Roentgenol. and Rad. Ther., March, 1936, **35,** 359–370.

Radical surgery followed by post-operative irradiation produces 72 per cent of 5-year cures when the breast alone is involved by malignancy, and 23 per cent of 5-year cures when the breast and axilla are involved. These figures compare with the generally accepted averages of 70 per cent of 5-year cures when the breast alone is involved and 20 per cent when both the breast and axilla are involved, if surgery alone is utilized.

In an article previously recorded the author shows 48 per cent of 5-year cures when the tumor was confined to the breast and no 5-year cures when the breast and axilla were involved in cases in which the entire treatment was radiation, both external and interstitial.

In the present study 117 cases of operable breast cancer, each with positive biopsy, have been treated pre-operatively, 65 cases with 200 kv. roentgen radiation and 52 cases by the 4-gram radium element pack, these cases being subsequently operated on after an average interval of about two months. Irradiation caused clinical reduction in the volume of the breast tumor in all cases. The axillary disease showed regression by the pre-operative radiation in only some of the cases. In the group of individuals treated by pre-operative roentgen radiation who were given 1,800 r per portal to each of five fields, 33 per cent showed microscopic disappearance of the breast lesion and 22 per cent disappearance of the axillary involvement. Those treated by the radium pack by 20,000 mc.-hr. per portal showed complete microscopic disappearance of the breast tumor in 14 per cent and in no case was there complete disappearance of the axillary involvement. With a larger dose of 24,000 mc.-hr., 45 per cent showed disappearance of the breast tumor and 13 per cent disappearance of the axillary involvement.

Sterilization of the ovaries in pregnant women with breast carcinoma and in all women under 35 years of age is urged.

The pre-operative radiation treatment of the breast should be tangential to the lung as much as possible in order to avoid radiation pneumonitis and secondary anemia.

J. E. HABBE, M.D.

Cancer of the Lip. A Marin. L'Union Méd. du Canada) January, 1936, **65,** 42–47. (Reprinted by permission from British Med. Jour., March 28, 1936, p. 52 of Epitome of Current Medical Literature.)

The author divides cancer of the lip into two distinct types: spinocellular and basocellular. The latter form has a slower growth and a lower grade of malignancy. It occurs on the upper lip and spreads locally; it then invades and destroys the neighboring and deeper tissues. Distant metastasis never occurs, and development is so slow that ten years may elapse before complications take place. There is no pain, and the general condition of the patient remains good. Death is not caused directly, but by hemorrhage brought about by the invasion of a blood vessel, by meningitis, or by erysipelas.

Spinocellular epithelioma involves the lower lip, develops very rapidly, and is of high-grade malignancy. Metastases are very common, and may be found in distant parts of the body. After one or two years the

patient usually succumbs to cachexia, marasmus, and general infection. Epithelioma of this type arises in the mucous membrane of the lip, and is often preceded by leukoplakia. The ulcerated growth is about the size of an olive. Cancer of the basal-celled type of the upper lip occurs on the skin and develops as a senile keratosis. The growth is small at first and grows very slowly; the glands are never invaded. Treatment of this form of epithelioma, when the growth is still localized in the skin, should be by electrocoagulation or radiotherapy. Treatment for growths of the spinocellular type is by radium needles and excision of the glands. If these glands are fixed and inoperable, deep radiotherapy is a palliative procedure. A case is recorded which was cured by radium.

The Treatment of Malignant Melanoma with Roentgen Therapy at Short Distance. H. Chaoul and K. Greineder. Strahlentherapie, 1936, **56,** 40.

After a brief discussion of the various treatment methods of malignant melanoma, *i.e.*, surgery, endotherm knife, irradiation, the authors report 14 cases treated by roentgen rays and observed during the last four years. They emphasize that while this type of tumor has always been considered highly radioresistant, in their experience this did not prove to be correct. They used massive doses of roentgen rays produced at moderate potentials and with fairly heavy filtration and at very short distance (below 10 cm.). With this technic it is possible to apply from 400 to 500 r per day and total doses of 10,000 r. The clinical data of the 14 cases are given in tabulated form. Although the number of cases is small and in view of the fact that they have been under observation from five months to four years only, no definite conclusions as to the efficacy of the method are drawn. However, the results are quite encouraging if one considers the high malignancy of melanosarcoma, and, therefore, this method should be given a trial in suitable cases.

ERNST A. POHLE, M.D., Ph.D.

The Roentgen Treatment of Malignancy Using Filtration Equivalent to 5 mm. Copper. E. A. Merritt and R. Rhett Rathbone. Am. Jour. Roentgenol. and Rad. Ther., March, 1936, **35,** 334–343.

For the fifteen months preceding the recording of this material the authors have been using a new filter composed of 1.25 mm. tin, 0.25 mm. copper, and 1.0 mm. aluminum for malignancy therapy, using 220 kv., 20 ma., 50 cm. distance, with an intensity of 10 r per minute measured in air. This composite filter has a maximum wave length as defined by Thoreaus of 0.21 Ångstrom, which is the same maximum wave length as filtered by 5 mm. copper. The effective wave length is 0.086 Angstrom. The intensity is 35 per cent greater with this composite filter than with 5 mm. copper filter. It is believed that there is a differential effect on the skin or epidermoid structures as a group, in contrast to connective tissue or supporting body structures as the opposite group. Therefore, by increasing the filtration there is better protection of the underlying subcutaneous tissues when giving a lethal skin dose. In cases in which blistering doses are given over large areas (15 × 5 cm. and over), the heavy filtration is necessary to insure healing. Widening of the lethal threshold between skin and subcutaneous tissues is not readily observable in cross-firing, as, for example, in treating malignancies of the head and neck, since it has been shown that the transmitted radiation is very "soft," even when high initial filtration is used.

The authors feel that protraction of treatment time in days increases the subcutaneous tissue tolerance but when the time is protracted too long, or approximately nine weeks, there is danger of tumor recovery. Hence the daily and total dose must be adjusted so as to exceed the recovery rate or the so-called tolerance dose, which is estimated by the writers to be about 150 r per day to a single area using heavy filtration. For the sensitive malignancies with a relatively high daily dose administered, the tumor may be destroyed in about three weeks' time. However, if the malignancy is relatively resistant the time should be protracted over four to six weeks with lower daily dose and higher total dose.

With the heavy filter now used the skin reaction develops slowly, complete destruction being not observed until the thirty-seventh day after beginning treatment. While there is complete vesiculation there is very little edema of the corium and practically no pain. Healing occurs in from six to twelve weeks. The authors cite cases of both superficial and deep-seated extensive malignancy treated by this method, with very favorable results extending over several years' post-radiation observation, with surprisingly little immediate constitutional or permanent local ill effects.

J. E. HABBE, M.D.

Post-operative Irradiation Following Radical Operation in Carcinoma of the Cervix. F. Friedl. Strahlentherapie, 1936, **55,** 457.

The value of x-ray therapy following radical operation (Wertheim) in patients with carcinoma of the cervix is still a debatable question and opinions for and against the procedure have been recorded in the literature. The author presents a material of 111 cases, all proved by biopsy: 40 were operated on only and 71 received x-ray deep therapy post-operatively. This consisted of one or two series, one shortly after the operation, the other three months later. Each series consisted of six fields of 10 × 15 sq. cm., applying a skin erythema dose over the entire small pelvis. The 40 cases treated in 1928 by operation only showed 42.5 per cent five-year cure, while the 71 cases treated in 1929 by operation plus radiation showed a 47.8 per cent five-year cure. Although the improvement in results due to the combined method is small, the author believes that roentgen therapy following radical operation in carcinoma of the cervix is of value.

ERNST A. POHLE, M.D., Ph.D.

Contribution to the Treatment of Incurable Carcinoma. J. Grode. Strahlentherapie, 1936, **55,** 462.

The author reports his preliminary results obtained with injections of chromic acid (CrO_3) in a solution of

1:10,000 in the treatment of inoperable advanced malignant tumors. As many as 35 injections of from 5 to 20 c.c. each were given subcutaneously, intravenously, or intraperitoneally without undesirable reactions. Occasionally arsenic acid (1:10,000) was also injected in doses of from one to two cubic centimeters. If the injections into the tumor itself proved painful, novocaine was added. There is no contra-indication to supplementary radiation therapy in cases treated by this chemical method. Although the author has only a few cases to report—he is a private practitioner without hospital facilities—he describes his method in detail and invites others with large clinical material to check his results.

ERNST A. POHLE, M.D., Ph.D.

Epicrisis of the Irradiated Carcinoma of the Cervix. H. Hausding. Strahlentherapie, 1936, **55,** 387.

Malignant tumors in patients presenting a similar clinical picture may show a great difference in their response to irradiation. Consequently investigators turned toward a study of the histologic structure in order to find a possible explanation for this observation. The author's own investigations are based on the microscopic examination of tissues of 240 cases of squamous-cell carcinoma of the cervix. By a careful correlation of the microscopic picture with the clinical data, certain conclusions could be drawn regarding the relation between histologic character and response to radiation therapy. The number of mitoses increased with the number of atypical structures in the tissue. Immature types of neoplasm did not offer a better chance for cure than more mature forms. Neoplasms with a high number of mitoses were slightly more radiosensitive than those with very few mitoses. However, no definite relationship could be discovered between response to treatment, percentage of cure, and histologic structure or number of mitoses in the neoplastic tissue. The microscopic picture should, therefore, be used only as one factor in arriving at a prognosis.

ERNST A. POHLE, M.D., Ph.D.

Results of Radiation Therapy of Carcinoma of the Vulva. I. von Kövesligethy Büben. Strahlentherapie, 1936, **56,** 28.

From 1919 to 1934, cases of carcinoma of the vulva to the number of 59 were seen at the Women's Clinic of the University of Budapest. Of these, 47 were inoperable. After biopsy, special radium applicators were prepared and applied at a distance from the skin of from 0.5 to 1.0 cm., filtered through 1 mm. Pt or its equivalent. The radium treatment was repeated if necessary in six weeks. The inguinal glands were subjected to roentgen therapy; three or four areas were given three times and a total dose of 1,500 r was administered (190 kv., 5 ma., 0.5 mm. Zn + 0.5 mm. Al, 30 cm. F.S.D.). Of the 47 patients, 38 with inoperable carcinoma of the vulva could be followed over a five-year period. Five remained well after that interval, corresponding to 13.1 per cent. One case was still well 11 years after the treatment. A palliative effect, that is, freedom from symptoms for at least one year, was seen in 30 cases.

ERNST A. POHLE, M.D., Ph.D.

COBRA TOXIN

Experiment with Cobra Toxin for Pain Relief. Johannes Seiler. München. med. Wchnschr., March 27, 1936, **83,** 527, 528.

A brief review of the French literature is given, and the claims as to the efficacy of cobra-toxin injection for relief of pain, particularly in carcinomatous metastasis, is discussed. In brief, the observers claim marked pain relief; regression of primary tumor, and experimentally, restraint of tissue culture growth. The author was unable to duplicate these results and concluded that in his experience, pain was not relieved and often made worse. Also, the regression of primary tumor was so slight as to be negligible. Other local and systemic untoward reactions occurred which were troublesome.

He is unable to explain the marked discrepancy between his own results and those of the French school, and particularly Calmette; but suggests that the organic extract he employed could possibly have had insufficient or no substance such as affords the salubrious results claimed.

WILLIAM R. STECHER, M.D.

CONTRAST MEDIA

Obliteration of Varicosities Studied in Roentgen Images. K. E. Herlyn. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1936, **53,** 122–131.

Following a brief review of previous experimentations concerning the roentgenologic demonstration of varicosities, the result of original experiments concerning 50 patients are reported. As obliterating and roentgenologic contrast medium a solution was used of Uroselectan B. and invert-sugar. The author studied particularly the time during which this medium could be demonstrated in the circulation, the distribution of the medium and the direction of its flow, the mechanism of evacuation, and external influences bearing on these phenomena. The results were obtained partly with, partly without, compression of the femoral vessels.

H. A. JARRE, M.D.

Injection of Thorotrast to Determine the Presence and Extent of Subphrenic Abscess. K. Heckmann and E. Altenburger. München. med. Wchnschr., Nov. 8, 1935, **82,** 1800–1802.

Thorotrast injected into a subphrenic abscess not only verifies the provisional diagnosis, but may actually demonstrate its etiology. This procedure is valuable, particularly when a gastro-intestinal study is precluded. The authors consider this method superior to air injection, after attempt at complete drainage of the abscess cavity, which is generally impossible. The thorotrast, by virtue of its radio-opacity and high atomic weight,

lends itself admirably for outlining the various recesses and dependent portions of the collection. No toxic effects were manifest. By rotating the patient the entire inner relief of the abscess cavity can be visualized, and roentgenographically recorded.

A case is presented in which a diagnosis of subphrenic abscess was established, and additional suggestive evidence of an indeterminate density in the vicinity of the gall bladder. Autopsy study revealed the latter density to be a carcinoma arising from the gall bladder, which had ruptured and extruded numerous biliary calculi, and had invaded the transverse colon to some degree. The latter infectious process accounted for the fecal odor of the aspirated pus. The authors are of the conviction that an earlier examination employing an opaque enema would have depicted definite alteration in the mucous membrane relief pattern at the site of the infiltrating neoplasm, which possibly would have suggested the correct diagnosis.

In evaluating the procedure of thorotrast injection into suspicioned subphrenic abscesses, the authors consider it to be a safe and simple procedure, affording information as to the extent of the abscess cavity and possibly its etiology, without necessitating the complete drainage of the cavity—which generally is not feasible. The information obtained is an aid to the institution of the proper therapeusis. This method is advocated for other abscess cavities such as psoas abscess.

WILLIAM R. STECHER, M.D.

Extravasation of Pyelographic Contrast Media into the Retroperitoneal Connective Tissues. K. Heckmann. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1935, **52,** 601–606.

During instrumental pyelography extensive extravasation of the contrast medium occurred from the renal pelvis into the surrounding fatty capsule and the loosely textured retroperitoneal connective tissue. There was neither an appreciable degree of hydronephrosis nor any serious pyelonephritis. The patient succumbed to a lobar-pneumonia. Definite evidence of rupture of the renal pelvis could not be demonstrated at autopsy.

H. A. JARRE, M.D.

Cholangiography for the Study of Biliary Tract Disease. J. A. Saralegui. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1935, **52,** 571–579.

The author has studied the biliary tract during the last ten years by injection of contrast media into postoperative biliary fistulæ. He first reported on his findings in 1930; further, in 1933 and 1934. During the earlier investigations lipiodol was used which, however, was found somewhat objectionable in the bile passages. In later years he has used thorotrast, which has proved to be a very satisfactory medium. Eleven excellent illustrations show the value of this method and demonstrate various degrees of dilatation of the common duct with inflammatory changes in the wall, residual calculi in various bile passages, stasis, and dysfunction. There can be no doubt that in persistent biliary fistulæ a roentgenographic exploration as practised by this author can be of great help for diagnosis and indication for operative cure.

H. A. JARRE, M.D.

A Case of Fracture of the Temporal Bone with Air in the Ventricles. Semsettin A. Üstel. Röntgenpraxis, December, 1935, **7,** 816–818.

According to the literature, only 31 cases of pneumatocaphalus following fractures have been described. In most of these cases, the fracture extended into the middle ear and there was a perforation of the ear-drum. In a case described by the author a fracture of the temporal bone extending into the petrous portion was demonstrated, and the ventricular system was filled with air and looked like an encephalogram.

HANS W. HEFKE, M.D.

Experimental and Clinical Investigation Concerning Roentgenographic Demonstration of the Cerebral Surface. K. Koshimizu. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1936, **53,** 25–30.

By sub-occipital puncture and following removal of a corresponding amount of cerebro-spinal fluid, small amounts of thoratrast—0.3 c.c. per kilogram of body weight in dogs, 20 c.c. in adult humans—were introduced and roentgenographic records of the skull obtained at various periods thereafter. A very satisfactory delineation of the cerebral fissures thus could be obtained. However, while in animals no serious complications were observed the reactions obtained in two humans were such that the method could hardly be recommended for more general use.

H. A. JARRE, M.D.

CYSTICERCUS

Multiple Cysticerci in Man. Eleonore Schick. München. med. Wchnschr., April 24, 1936, **83,** 694–696.

The presence of the larval form of *Tænia solium* (pork tapeworm) in man is rare. The pig is the usual intermediate host for cysticerci, man occasionally usurping that rôle when ova enter the stomach. The embryos are distributed *via* the blood stream, to numerous organs, particularly, subcutaneously and intramuscularly, to the central nervous system and the orbit. Symptoms vary according to the site of involvement. The organism reacts by enveloping cysticercus with calcific deposition. Eosinophila is marked. It is important to obtain stereoscopic roentgenograms of such regions as the skull and the chest, to determine whether calcific stipplings are extra- or intra-cranial, or pulmonically located. The author sites a case of extensive cysticercus involvement of the entire musculature of the body and, in addition, intra-cranial and intrapulmonary. No cysticerci were found in the orbit, however. Incidentally this is the first case in which cysticerci were demonstrated within the lung *intra vitam*. The calcifications are sharply circumscribed and 1.0 × 0.5 centimeter in size.

WILLIAM R. STECHER, M.D.

THE DIAPHRAGM

A Rare Case of Eventration of the Diaphragm. W. Wenig. München. med. Wchnschr., April 24, 1936, **83,** 693, 694.

The author reports an unusual case of marked eventration of the left diaphragm occurring post-operatively from an incision of suppurative cervical lymphadenitis. The paresis of the phrenic nerve was either resultant of damage to the phrenic nerve during the incision, or to cicatricial contracture about the nerve. The degree of relaxation of the diaphragm is noteworthy, inasmuch as the commonly employed phrenico-exeresis rarely approaches such a degree. The cause of this, he is unable to explain.

WILLIAM R. STECHER, M.D.

DOSAGE

The Effect of Roentgen Rays of Different Wave Lengths and Intensity on the Autolytic Ferments in Cancer Tissue. A. Faragó. Strahlentherapie, 1936, **55,** 481.

Cancer cells obtained from human cancer of the breast were suspended in solutions with a p_H of 3.8 and 8.0, respectively, because these two values represent the optimal C_H for pepsinase and trypsinase. Two qualities of roentgen rays were used: 180 kv., 0.8 mm. Cu + 0.5 mm. Al, and 100 kv., 1.0 mm. Al. The respective half value layers in copper amounted to 1.18 mm. and 0.13 mm. The action of the ferments is increased following irradiation up to a dose of 2,500 r; after further increase of the dose it is decreased. The wave length of roentgen rays has no influence on this reaction. The effect of radiation is, however, dependent upon the intensity, higher intensity having a more pronounced effect provided that equal doses are given. In order to determine the mechanism of the observed phenomena, 0.25 per cent solutions of pure ferments were irradiated. It appeared that they are due to a direct effect of roentgen rays on the autolytic ferments.

ERNST A. POHLE, M.D., Ph.D.

The Sensibilization of Roentgen-resistant Neoplasms by Means of Short Electric Waves. G. Fuchs. Strahlentherapie, 1936, **55,** 473.

This is a preliminary report regarding the combined application of short electric waves and roentgen therapy. The author states that short electric waves do not increase the degree of malignancy in a neoplasm. There are also no injuries to the skin area to be expected from the combined application of roentgen rays and short electric waves. While he is not prepared to state definitely how much benefit may be derived from this combined treatment, he suggests that it be given a trial in suitable cases.

ERNST A. POHLE, M.D., Ph.D.

ELECTRICAL EFFECTS

Radiation and Electric Charges in the Atmosphere. F. Dessauer. Strahlentherapie, 1936, **55,** 614.

This is a report rendered by the author before the Thirteenth Congress of Roentgenologists and Radiologists of Czecho-Slovakia, held in Prague in 1935. He analyzes the relation between climate and biologic reactions. The rôle played by electric charges in the air as suggested by the author's researches is discussed in detail. Its clinical application is the inhalation of air charged with negative ions in an attempt to influence beneficially certain pathologic conditions. (For details, see the author's book, "Zehn Jahre Forschung auf dem Physikalisch-Medizinischen Granzgebiet," Georg Thieme, Leipzig, 1931.)

ERNST A. POHLE, M.D., Ph.D.

EPIDIDYMIS

Hemangioma of the Epididymis. A. L. d'Abreu. British Jour. Surg., April, 1936, **23,** 858, 859.

It would seem rather difficult to diagnose pre-operatively this condition from other cystic and inflammatory swellings of the epididymis. A record of the reported case is incorporated in the article, along with reproductions of the microscopic sections.

DAVIS H. PARDOLL, M.D.

EPILATION OF SCALP

The Epilation of the Scalp by Roentgen Rays. A. Proppe. Strahlentherapie, 1936, **55,** 225.

The author has investigated the various methods recommended for epilation of the entire scalp based on clinical observations and mathematical deductions. He comes to the conclusion that most methods in use to-day are fraught with danger. The application of five or more fields leads to overlapping and consequently to appreciable overdoses in some areas. The method of Schreus, who uses only four fields and a focal skin distance at least as great as the diameter of the skull (100 kv., 0.5 mm. Al; 400 r per field), seems to be the safest procedure and produces uniform results. Photographs showing the scalp of a patient treated by this method are shown in the article.

ERNST A. POHLE, M.D., Ph.D.

Studies of Late Effects Following Epilation by Roentgen Rays, Especially Regarding the Mental Development in Children. T. Symann. Strahlentherapie, 1936, **55,** 248.

During the period from 1917 to 1926, a total of 312 roentgen epilations were carried out at the University Skin Clinic in Dusseldorf. The author conducted a follow-up study in order to determine whether or not there were any late injuries in these patients. He was particularly interested to investigate the possibility of an influence of irradiation on the development of the young brain. Fifty-three cases were available for study; 33 were treated for tinea, five for favus, eleven for trichophyton, and four had an undetermined

diagnosis. In four patients the hair grew thicker following epilation; in eight it appeared to be thinned out; in one case there was definite atrophy of skin and bone which the author believes was probably due to an error in dosage. In eight instances the new hair was darker, in two of a lighter color than before epilation. Curly hair grew in 14 children but straightened out after from a year to 18 months. One patient, aged two years and ten months at the time of roentgen epilation, has been complaining of headaches and vertigo since. One might consider in this particular case an injurious effect of roentgen rays because of the great radiosensitivity of the young growing brain. The intelligence test showed figures below normal in 18 patients. An analysis of the entire material, however, did not offer definite proof that the roentgen epilation affected the intelligence of the treated children.

ERNST A. POHLE, M.D., Ph.D.

GASTRO-INTESTINAL TRACT (DIAGNOSIS)

Pneumatosis Cystoides of the Intestine. Erich Forfota. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1936, **53,** 131–139.

This paper contains the report of a case of this rare affliction which was orginally published by Ruckensteiner and Kux. Symptoms of a perforated ulcer were so predominant in this patient that the roentgenologic diagnosis of pneumatosis cystoides was not made, though the roentgenologic record published contained sufficient material for such a diagnosis. Characteristic symptoms are pneumoperitoneum, interposition of characteristically altered intestinal loops between liver and diaphragm, ascites, and the characteristic appearance of pneumatotic intestinal loops.

H. A. JARRE, M.D.